OCTOBER, 1936

BRAIN.

PART 3, VOL. 59.

THE CLINICAL PICTURE OF MINOR CORD LESIONS IN ASSOCIATION WITH INJURIES OF THE CERVICAL SPINE: WITH SPECIAL REFERENCE TO THE DIAGNOSTIC AND LOCALIZING VALUE OF THE TENDON REFLEXES OF THE ARM (INVERSION OF THE RADIAL REFLEX).

BY F. M. R. WALSHE AND JEAN ROSS.

(*From the Department of Neurology, University College Hospital.*)

INTRODUCTION.
THE PRODUCTION OF THE VERTEBRAL INJURY.
THE CLINICAL PICTURE.
INVERSION OF THE RADIAL REFLEX (BABINSKI).
SUMMARY.
APPENDIX.
REFERENCES.

INTRODUCTION.

THE immediate consequences of a severe but non-fatal injury to the cervical spine and cord are so dramatic that they present no diagnostic difficulty. The quadriplegia with priapism and retention of urine which ensues upon such an injury has long been familiar to the clinician.

It is also known that an injury, fracture or fracture-dislocation, of the cervical spine may be sustained without any associated lesion of the spinal cord.

Between these two extremes are those cases with which we are now concerned, namely, those in which the spinal cord does sustain some relatively slight damage, either a momentary nipping when there is displacement of cervical vertebræ in relation to one another, or a momentary stretching over the posterior aspect of the vertebral bodies when the head is forcibly flexed, as in a fall in which the vertex strikes the ground first.

With the pathological changes produced in the cord in this way we are not here especially concerned. Indeed, no dogmatic statement can be made about them since the cases in question do not come to autopsy. But we believe that the clinical picture resulting from injuries of this less severe type has not been adequately described, is not uncommon, and is usually unrecognized.

Of the six cases which form the material of the present account, only one had been recognized, though more than one of them had been submitted to neurological examination. The diagnoses actually made included progressive muscular atrophy, amyotrophic lateral sclerosis, primary lateral sclerosis, and arthritis of the shoulder.

It has therefore seemed worth while to give a brief account of the clinical picture presented by these minor injuries of the cervical cord, since it is a recognizable picture, and when found in association with a history of injury leaves little room for error of diagnosis. Paradoxically, however, it is this history of injury which is in a measure responsible for directing attention away from the cervical spine and cord, since it is the head which first receives the violence and not the neck.

The Production of the Vertebral Injury.

In an analysis of spinal injuries, to which the reader is referred for details, Jefferson [4] has drawn attention to a number of points which are of importance in our present connection. He emphasizes that fractures and dislocations of the cervical spine are commonly produced by violence directed against the head. In other words, head injuries are the usual cause of injuries of the cervical spine. The original trauma may be trivial, but it acts by producing excessive flexion (anterior or lateral) of the cervical spine. In the majority of such cases the fracture or dislocation occurs between the 4th and 5th, or between the 5th and 6th vertebrae. The latter is probably the more common level.

All of the six cases which form the basis of the present account were cases of head injury primarily. All sustained scalp wounds, abrasions or contusions of the scalp. Four were rendered transiently unconscious, and the remaining two were transiently "dazed." In one case the patient was struck on the head by a motor car. One patient ran his head violently against a goal post while playing football. Three fell from small heights striking the head first on reaching the ground, and one slipped when entering a room, lurched and fell forwards, striking his head violently against a hot-water pipe near the floor level.

Jefferson cites a typical case in which, as in these, attention was not unnaturally directed to the head injury. A bale fell from a height, felling a man who stood beneath it, rendering him unconscious and inflicting a scalp wound. When he recovered, the paralysis of his right arm which then became apparent was thought to be due to a contre-coup lesion of the left motor cortex. In fact he had sustained a fracture of the 5th cervical vertebra and an injury to the brachial plexus.

It is, then, clearly important in cases of head injury to bear in mind the possibility of damage to the cervical spine and cord, more especially if the patient subsequently complains of pain or stiffness in the neck.

The Clinical Picture.

For the reasons mentioned, and also from the fact that in the type of case under consideration the paralysis of the limbs is not very severe or profoundly disabling, attention is usually not drawn immediately to the spinal or cord injury. If the patient happens to have been concussed and to have been confined to bed for some time, it may not be until he gets up and begins to resume activity that his attention is drawn to disabilities that he may not previously have noticed, or that he may have attributed to his general condition.

In some instances where consciousness has not been lost at the moment of injury, as in Case 2 in the Appendix, the patient complained at once of a "dead feeling" from the neck downwards, while another (Case 4 in Appendix) continued to complain of tingling in his hands, and of accesses of tingling running down his arms and legs if he bent his head forward. These symptoms he had noted from the moment of regaining consciousness after his fall.

In one case only out of the six was there any disturbance of sphincter control. This patient (Case 1 in Appendix) was incontinent of urine and fæces for some three weeks after his accident, but as he was mentally considerably reduced it is difficult to assess the significance of these disorders.

The common story given by the patients is that when the resumption of activity begins after recovery from the immediate effects (e.g. concussion) of the injury, they find the arms alone, or both arms and legs weak. This weakness may persist unchanged, may gradually and partially clear up, or may even slowly increase with the passage of time. In our experience, it cannot be assumed that the relatively moderate degree of the initial disability means that complete recovery may be looked for within a short or measurable period.

The appearance of muscular wasting in the upper limbs is not invariable, and when it occurs may not be noticed by the patient for some weeks, but in one case (Case 1) it was already marked when he came under observation in the third week after the injury.

Systematic examination of the nervous system reveals the following signs :—

Cervical sympathetic.—Slight narrowing of the palpebral fissures with relative smallness of the pupil was observed in one case. In the remaining five there were no signs of a lesion of the sympathetic pathway.

Motor system.—In one case there was wasting of the spinati, deltoid, biceps and triceps on both sides, with free fibrillation of these muscles. In another there was wasting of this distribution on one side. In the remaining cases no unequivocal wasting of local muscle groups could be seen. Tenderness of the wasted muscles was present. In the cases with wasting of the deltoid there was marked weakness of this muscle, but the disability was aggravated by the development of arthritis in the shoulder joint in both cases. This was probably largely due to lack of movement in the joint following the injury, and the rapidity with which in a hemiplegia, particularly a left hemiplegia, a similar condition develops in the shoulder joint is familiar to neurologists.

The forearm muscles showed slight hypertonus with slowness and clumsiness of fine movements: in other words the arms presented the combined signs of upper and lower motor neurone lesions.

In the legs slight hypertonus of extensors and plantarflexors, with a trace of weakness of dorsiflexion on one or both sides, or no weakness at all, are all that was found.

Sensory system.—Contrary to what might have been expected no objective sensory loss was found in five of the six cases. In the sixth (Case 3) there was a strip of impairment of sensory acuity to light touch and to pin-prick on the ulnar side of the left forearm. It must be borne in mind, however, that all but one of the cases came under our observation only after the lapse of weeks or months from the date of the injury. It is possible that in some at least, sensory changes had been present at the outset.

Pain in the neck and pain radiating down one or both arms was commonly complained of, and it was said by the patients to be more severe in wet and cold weather. As already mentioned, a tingling sensation radiating down the arms was also complained of.

Reflexes.—Perhaps the most significant diagnostic information was

obtained from the study of the tendon reflexes of the arms. In the routine examination of cases of nervous disease relatively little interest is displayed in these, and the account given by Babinski of the form and meaning of what he has called "inversion of the radial reflex" [1, 2] is not as widely known as it should be.

Whereas in amyotrophic lateral sclerosis with which these cases of cervical cord injury are commonly confused, the tendon jerks of the arms are uniformly, and sometimes considerably, increased, in these traumatic cases the various tendon jerks of the arms are varyingly affected: some are increased, some diminished or abolished, and one—the supinator jerk—may be replaced by finger flexion (inversion of the radial reflex). Thus it is common to find the triceps jerks greatly increased, the biceps jerks normal or diminished, and the supinator jerk on one or both sides replaced as described.

It is this differential behaviour of the arm-jerks that indicates the presence of a focal lesion of the spinal cord in the region of the 5th cervical segment, the segment usually involved in this type of spinal injury.

In the lower limbs the knee and ankle jerks are commonly exaggerated and ankle clonus may be present on one or both sides. Extensor plantar responses were present bilaterally in four of the six cases. Both responses were flexor in the remaining two.

The abdominal reflexes were abolished on one side in one case (R. B.), but were intact in the remaining cases.

Gait.—All but one of the patients were able to walk unassisted, but some cases did so with a slightly spastic gait and the tendency to trip easily and fall heavily that such patients usually show. One patient (Case 1) had been confined to bed since his injury and had not yet got up when he was under our observation.

Sphincters.—The patient just mentioned had incontinence of urine while under observation. In the remaining cases there was at no time any disturbance of sphincter control.

The cervical spine.—In all the cases there was manifest limitation of rotation of the head, with complaint of pain when the limit was reached if the effort to turn further was sustained. The limitation was not always equally marked in rotation to the two sides. Some limitation of extension of the neck was also present. Lateral flexion was usually both painful and limited. Two of the patients held the head stiffly at all times and thrust slightly forwards.

In one case only did a radiogram give unequivocal evidence of dis-

placement of vertebræ. In Case 4 there was clear narrowing of the intervertebral spaces between C 5, 6 and 7. In the others some degree of arthritis was present, but perhaps not more than was compatible with the age of the subject, for most of them were fifty years or over.

In short, the essential elements in the clinical picture are as follows: (*a*) Limitation of movement of the head and neck, with pain and stiffness on movement. (*b*) Some general weakness of the upper limbs, sometimes associated with special weakness and wasting of muscles supplied by the 5th and 6th cervical segments. Some hypertonus and slowness of movement may also be found. (*c*) Characteristic differential changes in the tendon-jerks in the arms, usually including inversion of the radial reflex. (*d*) Slight hypertonus of the extensor group in the legs, with increased knee and ankle jerks, and in some cases ankle clonus and extensor plantar responses. Slight weakness of dorsiflexion and a spastic gait may also be seen. (*e*) An absence of sensory loss, at least at the time at which the cases have come under our observation. There was a single exception to this generalization (Case 3). (*f*) Absence of defects of sphincter control. (*g*) Slow and imperfect recovery.

Inversion of the Radial Reflex (Babinski).

This phenomenon was described by Babinski in 1910 [2] as follows: "Nous avons dit que la percussion de l'extrémité inférieure du radius provoque toujours, à l'état normal, une flexion de l'avant-bras sur le bras. Celle-ci s'accompagne parfois d'une flexion de la main et des doigts: mais ce dernier mouvement, chez l'individu sain, a une intensité qui est généralement inférieure à celle de la flexion de l'avant-bras sur le bras et ne lui est jamais supérieure. Or, la diminution ou l'abolition du reflexe de flexion de l'avant-bras, état pathologique, peut avoir cette conséquence que la percussion de l'extrémité inférieure du radius détermine une flexion de la main et des doigts l'emportant en intensité sur la flexion de l'avant-bras ou se produisant alors que celle-ci fait défaut. C'est ce phénomène que j'ai décrit sous la dénomination d'*inversion du reflexe du radius* et dont la réalité a été confirmée depuis par de nombreux observateurs."

This lengthy statement is perhaps necessary since in the rare instances in which the phenomenon is mentioned in English textbooks, it is inaccurately described. In any circumstances in which there is a general increase in the arm-jerks, as in a residual hemiplegia, or in amyotrophic lateral sclerosis or disseminated sclerosis, it is not unusual to find that on eliciting the supinator-jerk, or even the biceps jerk,

the appropriate response is accompanied by some reflex finger flexion. This is not inversion of the radial reflex, but it is so described in the textbooks in question and the term is thus deprived of any significance.

Discussing the localizing value of this inversion, Babinski ([1] p. 72) says that in lesions of the cervical region of the cord, the tendon-jerks of the lower limbs are uniformly increased, but that it is otherwise with the arm jerks the form of which depends upon the localization and length of the lesion. If it extend from the 5th to the 8th cervical segments all the arm-jerks may be abolished. With less extensive lesions not all the jerks may be abolished and inversion of the radial reflex may be seen. For this to occur three conditions are necessary: (i) there must be a lesion of the 5th cervical segment; (ii) the 8th cervical segment must be intact, (iii) there must be involvement of the pyramidal tract at a level higher than the 8th cervical segment.

As a rule, inversion of the radial reflex is accompanied by increase of the triceps jerk and by diminution of the pronator reflex (percussion on the front of the head of the radius, movement of pronation of wrist).

Pathologically, this phenomenon is most often seen in syringomyelia and in traumatic lesions and compression of the cervical cord.

Numerous examples of this inversion, with the verification of its segmental localizing value, are to be found in the pages of the *Revue Neurologique* during the period 1910-1915. Gendron has given a detailed account of this and other segmental signs in his *Thèse de Paris* [3].

We have, then, a clinical picture which is not that usually given as characteristic even of the slighter degrees of spinal cord injury. Thus, in the discussion on spinal injuries, Jefferson's contribution to which we have already cited, the account given by Riddoch [5] of the cord injuries is of a far graver type of injury than that we are now considering. The presence of sensory loss is assumed as constant, and the localizing indications obtainable from its upper level discussed. In short, this description gives no indication of the existence of the clinical type under discussion, and in so far as it purports to cover the ground of spinal cord injuries from cervical fracture and dislocation might almost be taken to exclude the occurrence of milder types than it describes.

It will be seen that there are many factors which militate against the recognition of these mildest forms of cord injury. The causative injury is ostensibly one of the head, the spinal cord symptoms may come

to notice only after an interval; when seen they are not of the kind usually associated with injury: that is, they lack sensory loss and sphincter disturbance amongst their number. For this last reason they are very apt to be diagnosed as indicating early amyotrophic lateral sclerosis, and the history of trauma is lightly swept aside as irrelevant.

It is in these circumstances that the careful examination of the tendon reflexes in the upper limbs becomes so important; is, in fact, the basis of an accurate diagnosis.

Further, these reflexes serve also to differentiate pure nerve root or plexus lesions from cord lesions. If the weakness and wasting corresponds to a lesion of the upper roots of the plexus, the presence of bilateral changes in the arm-jerks points to a lesion of the 5th cervical segment, either as the sole or as an associated lesion.

SUMMARY.

A brief account is given of the clinical picture of a relatively slight type of damage to the cervical cord associated with dislocation or fracture of the cervical spine. In this the initial disability is comparatively slight and there is neither sensory loss nor impairment of sphincter control. The original violence which causes the spinal injury is always applied to the head, and thus attention is easily diverted from the presence and nature of the essential lesion.

The condition is commonly diagnosed as amyotrophic lateral sclerosis, progressive muscular atrophy or primary lateral sclerosis, owing to the absence of sensory changes and of disturbances of bladder control. *The most important and most characteristic feature in the clinical picture is the differential behaviour of the tendon-jerks in the arms, and the common—though not invariable—presence of inversion of the radial reflex.* As Babinski has shown, this phenomenon indicates the presence of a focal lesion in the 5th cervical segment of the cord. It is seen in compression of the cervical cord, in syringomyelia and in the type of injury to the cervical cord now under consideration. It is not seen in system degenerations of the cord, in which the tendon-jerks in the arms tend to be uniformly affected.

An additional feature of the clinical picture is the presence of some limitation of movements of the head and neck (anterior and lateral flexion and rotation). In only one of the present series of cases did radiographic examination of the cervical spine reveal a dislocation, but this negative finding is not unusual in severe and unequivocal cases of

cervical spine dislocation with grave paraplegia. A normal skiagram does not, therefore, invalidate the diagnosis of injury.

Some authorities believe that amyotrophic lateral sclerosis may be traumatic in origin, but in view of the condition we have described it is permissible to wonder what proportion of cases so diagnosed are, in fact, cases of true amyotrophic lateral sclerosis.

In the Appendix six illustrative cases are described.

APPENDIX.

Case 1.—R. B., farm labourer, aged 65. (U.C.H., 1936.)

History.—Fell from the top of a hay cart to the ground, striking the left side of his head and his left shoulder. Was dazed, but did not lose consciousness. Complained at once of loss of power in both arms. Taken to local hospital and found to be weak in all four limbs. While in this hospital he was incontinent of urine and fæces.

Examination (twelve days later).—Patient is confused mentally and a bad witness (has previously been an inmate of a mental hospital). He complains of pain in his neck and radiating down both his arms. Cranial nerves and cervical sympathetic normal.

Upper limbs.—There is profound weakness of the left arm, especially of deltoid, triceps and biceps. He cannot raise the arm off the bed, and the grasp is feeble. The right arm and the left forearm show some slight general wasting. There is moderate weakness of the right arm in all movements. The deltoid, triceps and biceps fibrillate freely on both sides. The dorsum of the left hand is œdematous.

Lower limbs.—No wasting, slight weakness of dorsiflexion, general extensor hypertonus of slight degree in both legs.

Sensory.—No trace of sensory impairment for any form of sensation can be detected on trunk or limbs. No complaint of paræsthesiæ in arms or hands.

Reflexes.—Jaw jerk absent.

	R.	*L.*
Biceps jerk.	Diminished.	Diminished.
Triceps jerk.	Increased.	Increased.
Supinator jerk.	Absent (replaced by finger flexion).	Diminished (with brisk finger flexion).
Knee jerk.	Brisk.	Brisk.
Ankle jerk.	Brisk.	Brisk.
Abdominal reflexes.	Normal.	Diminished.
Plantar responses.	Extensor.	Extensor.

During the three weeks this man remained under observation, he was kept in bed, as he was generally feeble, demented and dirty. Whether his incontinence could be related to his spinal injury or not is uncertain.

An X-ray of his cervical spine revealed the presence of arthritis but no sign of injury.

The case is included, although the injury was more severe than the others of the series, because although seen within two weeks of a manifestly fairly severe cord lesion, there was no sensory loss.

Case 2.—J. H., a carpenter, aged 61.

History.—Had always enjoyed good health. For some years had ridden 12 miles daily on his cycle to and from work.

In January, 1932, when entering a room, he slipped, lurched forwards and fell, striking his head violently against a hot water pipe which ran round the room about a foot from the floor. For a few moments he lay on the floor, dazed and feeling "dead from the neck down." He was helped to his feet, and taken for first aid treatment to the local hospital. Remained there overnight and then went home by bus.

Two days later he returned to work, travelling by bus. His legs felt dead and he could not guide them properly. His arms were weak and clumsy, and from the day of the accident he had been unable to mount or to ride his cycle. He could walk slowly and laboriously.

General examination.—The patient held his head stiffly when standing and walking. The range of rotation, flexion, extension and lateral flexion was restricted—that of rotation most severely. Optic discs and cranial nerves were all normal. Jaw jerk was absent.

Upper limbs.—Slow and clumsy in all movements. Power diminished in all movements. Could not elevate either arm to the vertical. Hand movements particularly clumsy. Isolated movements of the digits lost. No localized muscular wasting, but arms thin throughout.

Lower limbs.—Slight hypertonus of the extensors, but no definite weakness.

Sensory system.—No trace of loss or impairment of any mode of sensation in limbs or trunk.

Reflexes.—Jaw jerk absent.

	R.	*L.*
Biceps. Supinator.	Both absent and replaced by finger flexion.	Both normal.
Triceps.	Increased.	Increased.
Knee.	Increased.	Increased.
Ankle.	Increased. (Transient clonus on both sides.)	Increased.
Abdominal.	Feebly present on both sides.	
Plantar responses.	Extensor on both sides.	

Gait.—Spastic and laboured.

Radiogram of spine.—Arthritis, no sign of injury.

Case 3.—M. A., a nurse, aged 50. (U.C.H., 1936.)

History.—Knocked down by motor car while dismounting from a tram. Unconscious, regaining consciousness in hospital in an hour or so. Had a bruise on forehead and another on the point of the left shoulder. The left side of the head was tender for some days.

Since the accident has complained of pains in the neck, aggravated by any rotation of the head. Pain radiating down both arms, and numbness on the inner side of the left forearm and hand.

Many symptoms of a traumatic neurosis developed in the ensuing weeks, e.g. fear of traffic, sleeplessness, depression, nervousness, &c.

Examination (four months later).—Cranial nerves and cervical sympathetic normal.

Upper limbs.—Very slight wasting of the interossei of the left hand, with some tenderness of these muscles and weakness of movements employing them. This weakness was but slight, and in other respects the arms were normal.

Lower limbs.—No abnormality.

Sensory system.—Slight blunting of acuity to cotton-wool touch and to pinprick on the ulnar side of the left forearm, and just extending on to the hypothenar eminence.

Reflexes.—Jaw jerk absent.

Coracoid reflex (i.e. percussion over coracoid)

	R. Brisk, general flexion of arm.	*L.* Diminished.
Biceps.	Brisk.	Normal.
Triceps.	Very brisk.	Very brisk.
Supinator.	Very brisk (no finger flexion).	Normal (with brisk finger flexion).
Knee.	Brisk.	Brisk.
Ankle.	Brisk.	Brisk.
Abdominal.	Normal.	Normal.
Plantars.	Flexor.	Flexor.

Gait.—Normal. *Cervical spine.*—Movements limited and painful.

In this case the change in the left supinator jerk, which was verified by examination upon a later occasion, provided the only wholly unequivocal sign in a patient whose neurotic state rendered the assessment of her motor and sensory signs difficult.

Case 4.—J. E., engineer, aged 52. (U.C.H., 1936.)

History.—Fell from a step-ladder when standing 6 feet above ground level, striking the top of his bald head on the edge of an open furnace door. Was unconscious for some minutes. Sustained a long scalp wound, sagittally across the vertex. The wound was stitched and healed well. Since the accident he has had almost constant "nagging" pain in the neck and the back of the head. This pain runs down both arms, and in addition his hands feel as though he was "holding the terminals of a battery." This tingling sensation is worse whenever he bends his head forwards, and persists undiminished six months after the accident.

Both arms feel weak, but the left arm and hand are much weaker and more painful than the right. The weakness seems to have increased and now he cannot lift the left arm above the shoulder, and the effort to do so provokes severe pain in the shoulder.

Of his legs he makes no complaint, and he has been up all day and on his feet since his scalp wound healed.

General examination.—Long healed and pigmented scar of scalp wound. Rotation and flexion (anterior and lateral) of neck is markedly limited in range, especially rotation of the head to the left, and effort to exceed the range is painful. Active and passive movement of the left shoulder is greatly limited and there are clearly adhesions in the joint.

Cranial nerves and cervical sympathetic normal.

Upper limbs.—There is marked wasting of the left deltoid, and the left upper arm is three-quarters of an inch less in circumference than the right. The spinati are also slightly wasted. All movements of the limbs are of less than normal power, and the deltoid is not only wasted but is very weak. The right arm is thin, but shows no local muscular wasting. There is no fibrillation in either arm.

Lower limbs.—No abnormality. Walks normally.

Sensory.—No objective impairment of sensation on trunk or limbs.

Reflexes.—Jaw jerk absent.

	L.	*R.*
Biceps.	Diminished.	Normal.
Triceps.	Diminished.	Normal.
Supinator.	Diminished (finger flexion brisk).	Normal.
Knee.	Normal.	Normal.
Ankle.	Normal.	Normal.
Abdominal.	Sluggish.	Sluggish.
Plantars.	Flexor.	Flexor.

Wassermann reaction negative in blood and cerebrospinal fluid.

X-ray.—Marked narrowing of intervertebral space between C. 5, 6, 7.

Case 5.—T. S., a labourer, aged 33. (U.C.H., 1936.)

History.—Ran heavily against a goal post while playing football, striking his head. He fell momentarily unconscious, as he believes. On coming round, he had to be helped to his feet and was just able to walk, when supported on both sides, to an adjacent seat. Was taken home by car. Was then assisted to hospital, feeling " numb from the waist down " and as though his feet were too large for him. Was discharged from hospital after five days, and was then able to walk alone, but not with normal strength. Since resuming activity, he has found that whenever he bends his head forwards a feeling " like an electric shock " runs down the back of his legs and down his arms. He now feels perfectly strong again, apart from a feeling of stiffness in the left arm.

Examination (five months later).—Slight limitation of rotation of head, with a little pain at the limit of movement. Flexion of the head forwards provokes the " electric shock " feeling mentioned above.

Cranial nerves and cervical sympathetic normal.

Upper limbs.—Doubtful wasting of left deltoid, and suggestion of stiffness in movements of the left arm, but no weakness of either arm. No fibrillation.

Lower limbs.—No abnormality, walks normally.

Sensory.—No abnormality.

Reflexes.—Biceps. *R.* Brisk. *L.* Brisk.
Triceps. Very brisk. Very brisk.
Supinator. Brisk. Brisk.
(Both with extremely brisk finger flexion.)
Knee and ankle jerks normal on both sides.
Abdominal reflexes normal on both sides.
Plantar responses normal on both sides.

Wassermann reaction negative in both blood and cerebrospinal fluid. The latter being normal in all respects.

X-ray of cervical spine: nil abnormal.

In this case, a slight, but constantly observed, abnormality in the arm jerks is all that remains.

Case 6.—M. D., a married woman, aged 62. (1935.)

History.—Was knocked down by a car when crossing the street. Was unconscious until next day. Scalp wound on forehead, damage to nose and bruises on the right shoulder. Remained confused for some days, and was in bed in hospital for a month.

When she began to get up and to move about she found that she could not lift her arms properly, could not reach her head to brush her hair, the neck was very stiff and ached constantly. Aching pains ran down both arms, which slowly began to get thinner. Her legs also were stiff and walking was a labour. It took her over an hour to dress in the morning. At times, if she gets tired, both legs drag. At the time of coming under observation, the diagnosis was one of traumatic neurasthenia following a head injury.

On examination (six months after injury).—The head is held very stiffly, and rotation and anterior flexion are painful and very limited in range. She has to turn her whole body when she wishes to look to one side. The pupils are small, the palpebral fissures narrow, especially on the left side.

Upper limbs.—There is general weakness, slight general wasting, and slight hypertonus of both arms. Deltoids are specially weak, and she cannot elevate either arm to the vertical. All movements except this are possible, but are slow and a little clumsy. There is a suggestion of local wasting of the small hand muscles.

Lower limbs.—Slight general spasticity, slight weakness of dorsiflexion of both feet, with a tendency to drag the toes when walking.

Sensory.—No impairment of any form of sensation on trunk or limbs.

Reflexes.—Jaw jerk absent.

Biceps Triceps	*R.* Very brisk.	*L.* Very brisk.
Supinator.	Normal.	Normal.
	(Accompanied by brisk finger flexion on both sides.)	
Knee.	Very brisk.	Very brisk.
Ankle.	Very brisk. (Transient clonus.)	Very brisk.
Abdominal.	Present.	Present.
Plantar.	Extensor.	Flexor.

X-ray of cervical spine reveals severe arthritis.

During the eighteen months that this patient remained under periodical observation, she made a slow and imperfect recovery. The reflexes remained unchanged. Walking improved slightly, and the range of movement at the shoulders improved. The wasting of the small hand muscles appeared to increase for a few months, but finally became stationary.

REFERENCES.

[1] Babinski, J. "Œuvre Scientifique (Receuil des principaux travaux)." Masson et Cie., Paris, 1934. Pp. 51 and 72.
[2] *Idem.* *Bull. et Mém. de la Soc. des Hôp. de Paris*, 1910, **30**, 185.
[3] Gendron, A. *Thèse de Paris*, No. 229, 1913. Maloine et Cie., Paris.
[4] Jefferson, G. *Proc. Roy. Soc. Med.* (Sect. of Orthopædics), 1928. **21**, 21.
[5] Riddoch, G. *Ibid.*, 1928, **21**, 33.

TUMOURS INVOLVING THE VENTRAL ASPECT OF THE PONS AND MEDULLA, INCLUDING TWO CHORDOMAS.[1]

BY LEWIS D. STEVENSON, M.D., AND E. D. FRIEDMAN, M.D. (NEW YORK).

Introduction.

Two cases of tumour at the base of the brain were observed in the Neurological Service at Bellevue Hospital, a third was studied by one of us (L. D. S.) at New York Hospital, and the fourth occurred in private practice. All of the cases presented similar clinical signs and symptoms. The two cases observed at Bellevue Hospital had been diagnosed as possible tumours of the fourth ventricle. Two of the tumours described are of further interest because of the pathological findings. They were cases of chordoma, a tumour derived from the remains of the notochord.

Case Reports.

Case 1.—F. W., aged 33, housewife, was admitted to Bellevue Hospital on April 25, 1927. Her chief complaints were headache, blurring of vision, and pain in the back of the neck of two years' duration.

Previous history.—At the age of 14 the patient suffered from poliomyelitis, which left considerable weakness of the left lower extremity. Menstrual history was normal. There was an internal strabismus of the left eye, dating back to early life.

Present illness.—In December, 1924, the patient complained of numbness of the tongue, a feeling of pressure in the eyes, and blurring of vision. A year later she suffered from a dull "aching pain" over the vertex: she was operated upon for "sinusitis," but did not obtain relief. The headache continued. It was paroxysmal in type, began at the base of the skull, radiated forward and led to retraction of the head. Occasionally it was accompanied by vomiting. There were also periodic attacks of numbness of the tongue. One week prior to admission the patient suddenly lost consciousness. During the episode there was conjugate deviation of the eyes to one side, but no convulsion. In the latter part of 1926 and early in 1927 she suffered from outbursts of uncontrollable laughing. In February and March, 1927, she also complained of drowsiness.

[1] From the Neurological Service, Neuropathological Laboratory of Bellevue Hospital, and Department of Neurology of New York University, College of Medicine.

Case reports presented in part before the Section of Neurology and Psychiatry of the New York Academy of Medicine, October 11, 1932.

General medical state showed no abnormalities. Blood-pressure readings were 115/85.

Neural status.—There was bilateral papilloedema with hæmorrhages. Visual fields were normal. The pupils were normal. Palsy (old) of the left external rectus was found; no true nystagmus, but a few vertical jerks of the eyeballs upward. Right facial weakness and diminution of the corneal reflexes, especially the left, were noted. The lower jaw deviated to the left and there

FIG. 1.—Showing the tumour in Case 1. It measured 3·5 c.m. in diameter and was firmly adherent to the dura over the basilar portion of the occipital bone, just behind the sella. It is compressing the pons and the basilar artery, being attached firmly to the pons, more on the right side than the left. The tumour also compressed the Aqueduct of Sylvius, resulting in internal hydrocephalus and giving rise to papilloedema and headache. There was some compression and rotation of the medulla. The radiating streaks of an endothelioma can be seen in this figure. Microscopically it was a typical endothelioma of the meninges, with psammoma bodies in it.

was a mild left-sided nerve deafness. Palate innervation was impaired, especially on the right, and the gag reflex was lost. Innervation of the larynx was normal, and labyrinthine tests yielded normal responses.

There was weakness in the right grip and in the movements of both lower extremities, with atrophy of the peroneal and flexor groups, more pronounced on the left (poliomyelitic residua). The deep reflexes were more active on the right. The left Achilles jerk was absent. Abdominals were not obtained. The plantars were equivocal but Babinski's sign could not be elicited.

Sensation was intact in all forms. There was ataxia in the finger-to-nose test on the right. Gait was somewhat unsteady; there was a tendency to veer from side to side, more so to the right. Mental status showed no abnormalities.

X-ray examination of the skull proved negative. Blood chemistry figures and urine were normal.

The clinical impression was that of a neoplasm in the posterior fossa, involving the medulla and 4th ventricle.

Sub-occipital exploration with removal of part of the foramen magnum was carried out on May 3, 1927. The ventricles were aspirated and 60 c.c. of clear fluid under pressure was removed. The cerebellum was tense on both sides. There was very great thickening of the meninges. The cerebellar tonsils were jammed through the foramen magnum. No evidence of tumour could be found in the 4th ventricle. The surgeon concluded that we were probably dealing with a neoplasm in the medulla.

Patient died suddenly on May 7, 1927.

Post-mortem examination revealed a meningioma at the base of the brain (see fig. 1).

Comment.—The duration of symptoms in this case was about two years; headache and pain in the back of the neck were quite prominent features of the illness. The numbness of the tongue may well have been due to interference with one or both 5th nerves as they enter the pons, although the signs of 5th nerve involvement were slight. There was no nystagmus or evidence of serious involvement of the cerebellum. There was slight weakness in the legs and in the right grip (superimposed on the original poliomyelitic residua), but the Babinski sign was not present. It is conceivable that the sudden loss of consciousness, once recorded, might have been due to interference with the blood-supply of the brain through pressure on the basilar artery, although it might easily have been due to other factors. Apart from the very slight evidence of pyramidal tract involvement, there were few signs of pressure on long tracts; there was no loss of sensation over the arms, trunk or legs.

Case 2.—Emily M., aged 31, housewife, was admitted to Bellevue Hospital, February 2, 1932.

Her chief complaints were tinnitus, dizziness, unsteadiness in walking, and throbbing pain in the right occipital region for six months; pain in the right temporal region for five months.

Present illness.—For two months prior to admission the patient suffered from generalized headache, particularly severe in the frontal zone. For three weeks, there had been spells of vomiting preceded by nausea and accompanied by frontal headache. Diplopia came on at about the same time. At first it was only transitory, later constant. She also complained of roaring in the

ears, worse when she stooped forward, and more pronounced on the right. There was some impairment of hearing for four or five weeks preceding admission.

Neural status.—There was bilateral early papillœdema. Visual fields showed no abnormalities. Pupils were normal. No true nystagmus was found, but occasional vertical jerks upward. Weakness of the right 6th, impairment of bone conduction on the right, and absence of the gag reflex were noted. Bárány tests gave normal responses. The patient showed a tendency to fall backward and to the right, cerebellar ataxia on the right side, generalized increase of deep reflexes, and absence of abdominal reflexes. There was tenderness of the right occiput.

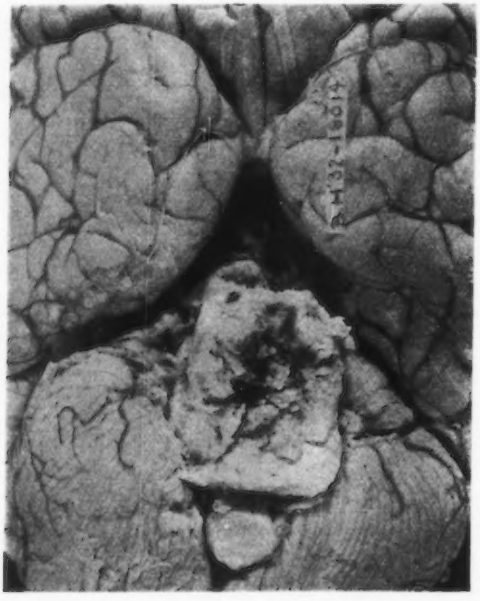

FIG. 2.—Showing the tumour of Case 2. It was 4·5 cm. long, 3 cm. wide, and 1·5 cm. deep. It was attached to the anterior surface of the pons and medulla in the middle line, but was somewhat thicker on the right side than on the left. It felt like soft rubber with spicules of bone over its surface. Sections of this tumour showed it to be a chordoma, and sections of the eroded bones of the skull underneath it showed chordoma cells in abundance.

She held her head in a fixed position, somewhat forward ("ceremonial attitude") and resisted anterior flexion. On two occasions she experienced difficulty in swallowing. The tongue felt stiff in its posterior part, and at times the patient found difficulty in speaking. When she voluntarily turned her head to the right, she experienced pain in the right occipito-cervical region.

The serological findings were negative, and X-ray examination of the skull showed no abnormalities except for a somewhat closed-in sella.

PLATE II.

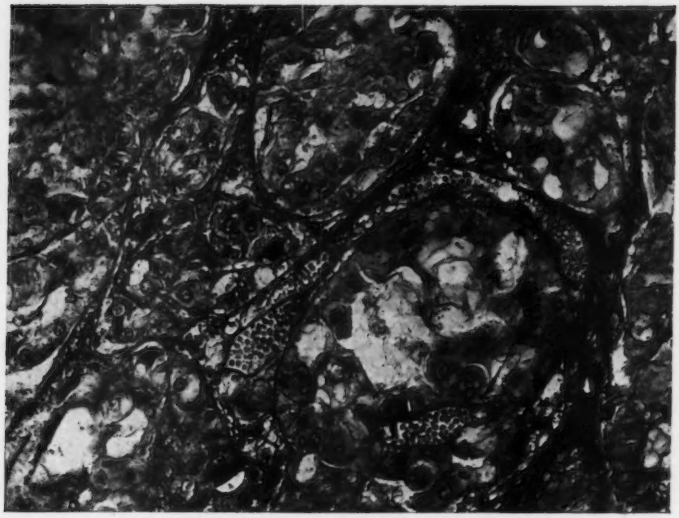

FIG. 3.—Showing the general microscopic appearance of the tumour with the cells separated by strands of connective tissue containing mucin and also denser fibrous tissue which stained pink with van Gieson's stain. The cells are large and contain many vacuoles or bubbles within their cytoplasm, and many contain more than one nucleus. The cells are, as a rule, not well defined individually in our sections, but form a sort of syncitial network which is well illustrated in fig. 4.

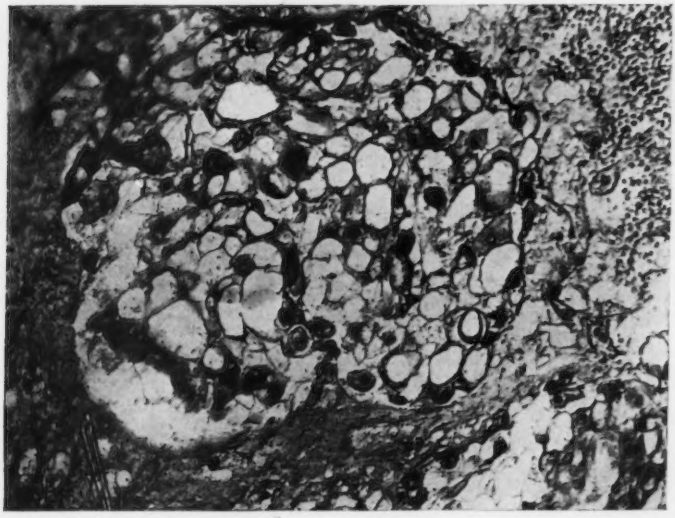

FIG. 4.—This figure also demonstrated the physaliphorous cells of chordomas. The bubbles or apparent vacuoles of those cells are said to contain mucin, although some pathologists have thought they were filled with glycogen. These physaliphorous cells are characteristic of this tumour, and are not found in degenerating cartilaginous tumours which are sometimes confused with chordomas.

To illustrate paper by Lewis D. Stevenson and E. D. Friedman.

On one occasion the patient volunteered the statement that when she turned toward the right she experienced peculiar movements in the tongue. These were accompanied by paræsthesiæ, especially at the tip. This symptom disappeared abruptly when she shifted her position. These " hypoglossal fits " recurred from time to time.

Throughout the patient's stay in the hospital her chief complaints were intense pain behind the right ear and dizziness induced by bending forward suddenly (modified von Bruns' sign).

The clinical diagnosis was tumour of the posterior fossa.

Sub-occipital exploration, first stage, was carried out first. Later, the second stage was performed. Ventricular puncture yielded fluid under great pressure. After exposure of the cerebellum, there was found an adhesive arachnoiditis at the base with loculation of fluid. The arachnoid was definitely thickened but the tumour was not found.

Owing to increasing stupor, and in order to exclude a lesion further forward with invasion of the mid-brain, ventriculography was carried out. It showed distended lateral ventricles and a globular 3rd ventricle. Because of the absence of quadrigeminal plate phenomena, this was considered confirmatory evidence of a lesion in the posterior fossa. Following this procedure, the patient showed horizontal and vertical nystagmus, paralysis of the right 6th nerve, weakness of the left, right facial weakness, and protrusion of the tongue to the right (without atrophy). Re-exploration of the posterior fossa with splitting of the vermis was then suggested and carried out. At this time there was found an accumulation of fluid in the midline within a cavity lined by a membrane. The aqueduct of Sylvius was found patent. No evidence of neoplasm was found.

Repeated ventricular taps were carried out for symptomatic relief (130 to 160 c.c. of fluid was withdrawn).

Patient died on June 11. Post-mortem examination revealed a growth lying on the ventral aspect of the pons and the medulla and attached to the clivus (see figs. 2, 3 and 4). It proved to be a chordoma.

Comment.—This patient presented symptoms for six months only. although the tumour had probably been there for a much longer period, There was only slight internal hydrocephalus in this case. The basilar artery was greatly compressed by the growth. The 5th nerve was not involved on either side, but both 6th and both 12th nerves were compressed by the tumour. The pressure on the 12th nerve probably accounted for the peculiar movements of the tongue when the patient turned on her right side.

Case 3.—M. Q., aged 31, housewife (from New York Hospital, service of Dr. George J. Heuer, to whom we wish to express our indebtedness for permission to report the case).

Her chief complaints were dull occipital headache, fairly constant, but with occasional exacerbations, dizzy spells, vomiting, blurred vision, spots before the

eyes, and staggering to the right on walking. These symptoms had been present for three months; they appeared after the delivery of a normal full-term child.

Examination showed an obese woman with tenderness in the occipital region and pain in the neck on flexion of the head. The patient was drowsy but normal mentally. Her vision was blurred and there was papillœdema with retinal hæmorrhages on both sides. Weakness of the right 6th nerve, with periodic diplopia, and a well-sustained lateral nystagmus, more pronounced to the right, were found. A clockwise type of nystagmus was present

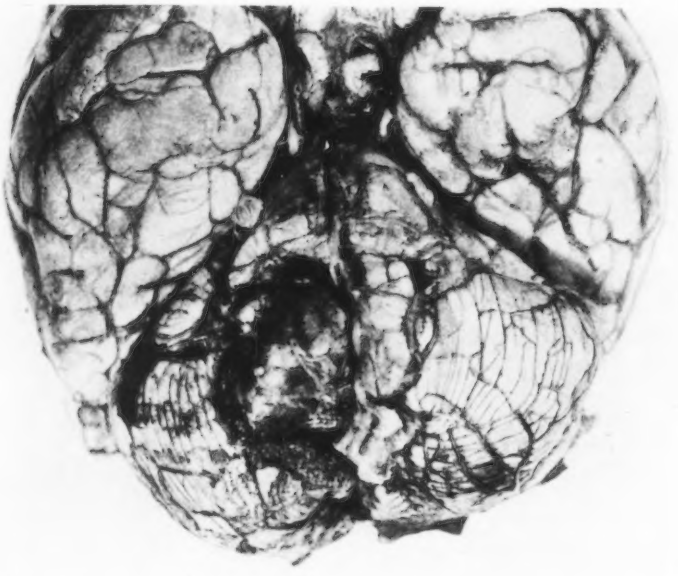

FIG. 5.—Showing the gross appearance and situation of the tumour in Case 3.

on looking upward and a counter-clockwise type on looking downward. Diminution of the right corneal reflex, hypoæsthesia and hypalgesia over the first and second divisions of the right 5th nerve were noted. Facial weakness, probably peripheral in type, was also present on the right side. Neither tinnitus nor deafness was complained of, and no deafness was demonstrated. Caloric tests gave normal responses on both sides. Speech was somewhat thick (dysarthria). The tongue was protruded to the right; showed no atrophy but some tremor.

The diagnosis of a right cerebellar neoplasm was made. Exploration was carried out on October 4, 1932, by Dr. George J. Heuer. A large nodular tumour was found close to the lateral recess on the right, dislocating the

brain-stem to the left. The patient did poorly, vomited dark coffee ground material, collapsed and died.[1]

Post-mortem examination revealed a tumour at the base of the brain on the right. There was a moderate degree of internal hydrocephalus with considerable hydrops of the 3rd ventricle. Sections of the tumour showed it to be a meningioma and the bone, removed from the region of the foramen magnum underneath the tumour, had been invaded by endothelial cells. The pituitary gland was somewhat enlarged, but not otherwise abnormal. The 7th and 8th cranial nerves on the right were very definitely compressed by the tumour. The 9th and 10th were apparently destroyed. The 5th nerve was not directly implicated on either side, but 5th nerve signs on the right may have been due to traction on this nerve when the brain-stem was distorted or dislocated to the left (fig. 5).

Comment.—The findings were those of a lesion at the base of the brain on the right with implication of the lower cranial nerves and the homolateral cerebellar pathways. The clinical syndrome was not that of an angle lesion.

Case 4.—This case is of interest because it could not be diagnosed in its earlier stages and because it also proved to be a chordoma. Further, the first and most outstanding feature of the case was a bilateral hypoglossal lesion with marked atrophy of the tongue; there were none of the classical signs of cerebral tumour.

A. W. P., a man, aged 59, was referred by Dr. Leander Shearer to one of us, (L. D. S.) because of dysarthria and difficulty in swallowing, noted first about August, 1931. This difficulty slowly increased and was later associated with pain in the back of the neck and in the occipital region.

Neurological examination in February, 1932, revealed atrophy of the tongue, more pronounced on the right side. There were no signs of pyramidal tract involvement, loss of sensation, choking of the discs or other signs of tumour within the skull. A diagnosis of bulbar palsy was made.

In May, 1932, the patient developed diplopia due to weakness of the left 6th nerve. Later, neurological examination revealed, in addition to weakness of the left 6th nerve, implication of the 10th and 11th cranial nerves, and the bilateral hypoglossal palsy already noted. There still was no evidence of pyramidal tract involvement or choking of the discs.

The patient was then lost sight of and died in another city in January, 1933.

Post-mortem examination revealed a tumour outside the dura at the base of the skull, invading the central part of the sphenoid bone and extending down through the base of the skull into the region of the posterior superior

[1] This may have come from an ulcerative lesion of the gastric mucous membrane, similar to the ulcerations described by Cushing, following lesion of a pathway leading from the mid-brain to the brain-stem and supplying trophic filaments to the gastric mucosa.

pharyngeal space. X-ray examination of the skull before the patient's death showed slight evidence of the presence of this growth. The tumour proved to be a chordoma.

Discussion and Differential Diagnosis.

The number of chordomas reported in the literature is about sixty. These neoplasms may grow from either end of the remains of the notochord. About an equal number from the region of the spheno-occipital synchondrosis and from the sacro-coccygeal region have been described. Only a few involving the cervical, lumbar and thoracic regions of the spine have been reported. These growths are usually not malignant, but if removed surgically tend to recur. Occasionally they give rise to metastases in other parts of the body. Ribbert, in 1894, produced these tumours experimentally by puncture of the intervertebral cartilages in animals. He suggested the name chordoma because he demonstrated that these growths were derived from the vestigial notochord.

A case reported by D. F. Cappell of Glasgow in 1928 showed, in places, the structure of the primitive notochord with primary and secondary sheaths surrounding the physaliphorous cells, thus adding the final proof that these tumours are actually derived from the notochord.

Chordomas occur more frequently in males than in females, and are found from the age of 16 up to 51 years or more.

One cannot establish a definite syndrome for tumours located in this region, but we believe now that signs of involvement of one or both hypoglossal nerves, or others of the lower cranial nerves, might help to place the tumour in front of the pons and medulla rather than in the 4th ventricle. Moreover, these tumours differ in several important respects from tumours invading the pons (e.g. glioma), from acoustic neuromas, and from tumours of the 4th ventricle.

Tumours of the 4th ventricle itself usually give rise to the von Bruns' sign (sudden vertigo with change in posture), signs of internal hydrocephalus with perhaps evidence of distant pressure on the chiasm owing to herniation of the floor of the 3rd ventricle. These cases, as a rule, are characterized by the absence of cranial nerve phenomena. The posture of the head frequently found in such instances is not always of the same type. We have encountered cases of tumour of the 4th ventricle which gave rise to forward displacement and flexion of the head in the typical "ceremonial attitude." One of us has observed this type of attitudinizing and fixation of the head in a case of teratoma

overlying the 4th ventricle (subsequently reported by Klenke and Brock). In other instances of similar localization there has been retraction and over-extension of the head with a tendency to the assumption of the attitude of decerebrate rigidity. We have recently had occasion to observe a case of ependymoma of the 4th ventricle with such retraction and over-extension of the head. One might say that, in general, posturing of the head is highly suggestive of a lesion in the posterior fossa, although we have on rare occasions encountered this symptom in cases of supratentorial growths. In cases of tumour involving the cerebello-pontine angle, the head is frequently tilted to one side with the chin directed towards the site of the lesion.

As has already been stated, there is no symptom complex characteristic of tumours at the base of the brain. Selinsky recently reported an instance of chordoma, somewhat further forward in localization than our own cases, in which optic atrophy, multiple ocular palsies, and erosion of the sella were found.

In a retrospective survey of our cases, one might say that the diagnosis of a ventrally-placed lesion is not easily made. The " hypoglossal fits " in one of our cases were, of course, exceedingly suggestive. Since the advent of careful encephalographic studies of the subarachnoid spaces, one would look for evidence of encroachment on the cisterna pontis. In the main, one would have to be content with a diagnosis of a lesion of the posterior fossa, and if the surgeon, on exploration, failed to find the lesion dorsally placed, it would be a prudent measure to explore the ventral aspect of the brain-stem for evidence of the growth. The surgical removal of these ventrally-placed neoplasms is, of course, not an easy matter.

Many of these tumours at the base are latent and symptomless, but they may involve any of the lower cranial nerves from the 8th to the 12th. They are frequently accompanied by disturbances in respiration and heart-rate, and the presence of intermittent glycosuria (phenomena due to the invasion of or contrecoup pressure against the 4th ventricle). Some of the more characteristic signs and symptoms include occipital headache, attitudinizing of the head, cerebellar ataxia, and an intermittent course.

The paræsthesia of the tongue described in one of our cases may have been due to stretching of the 5th nerve. The condition of the bone at the foramen magnum in Cases 2 and 3 might have given us a clue as to the localization, if careful radiographic studies of this region had been made, as was done in Case 4.

Ependymomas of the 4th ventricle are more apt to give rise to pain on turning the head, due to extension of the growth either upward from the spinal cord or downward from the 4th ventricle. This advance through the foramen magnum results in increase of the size of the brain-stem with tension on the meninges or the vessels.

Lesions of the cerebello-pontine angle are readily excluded by the presence of signs and symptoms referable to both divisions of the 8th nerve, characteristic nystagmus with the coarse component directed towards the side of the lesion, areflexia of the cornea and homolateral cerebellar signs. Vestibular tests on the side of the neuroma show definite impairment of function, sometimes even before deafness is noted.

Syphilitic meningitis at the base might enter into the differential diagnosis, but it is more apt to give rise to the picture of an angle lesion [2].

Atypical multiple sclerosis would be characterized by active remissions and exacerbations, more definite implication of the pyramidal tracts and posterior columns, and phenomena referable to the upper cranial nerves, especially the optic and those of the ocular muscles.

Infiltrating tumours of the pons (gliomata), as a rule, do not give rise to obstruction of the Aqueduct of Sylvius, hence there usually is no papillœdema. Headache is frequently absent, probably because there is no internal hydrocephalus. In our cases headache was an early and severe symptom; signs of pyramidal tract involvement are prominent features in glioma of the pons. They were practically absent in our first two cases. Involvement of the sensory division of the 5th nerve is more apt to be present in infiltrating tumours of the brain-stem owing to implication of the ascending spinal root. Nystagmus is also more frequent in intrapontine lesions. Pain in the neck is rare in glioma of the pons, but is pronounced in extrapontine tumours and occurs especially on movement of the head.

Vascular lesions of the pons and medulla are apt to give rise to more definite and clearly defined syndromes, involving either the distribution of the superior cerebellar artery, the posterior inferior cerebellar artery, the vertebral artery and the basilar artery with its branches.

We wish to express our indebtedness to Dr. Foster Kennedy for permission to publish the two cases from the Neurological Service of Bellevue Hospital.

REFERENCES.

CUSHING, HARVEY. "Intracranial Tumours," Springfield, 1932, p. 102.

FRIEDMAN, E. D., BROCK, S., and DENKER, P. "Syphilis of the Cerebello-pontine Angle," *Journ. of Syphilis*, 1933, **17**, 330-38.

FURLOW, L. T. "Intracranial Chordoma," *Arch. Neur. and Psych.*, 1935, **34**, 839-943.

MÜLLER, H. "Ueber das Vorkommen, von Resten der Chorda dorsalis bei Menschen nach der Geburt und über ihr Verhaltnis zu den Gallertgeschwulsten am Clivus," *Zeitschr. f. rat. Med.*, 1858, **2**, 202.

RIBBERT, H. "Ueber die Ecchondrosis physalifora spheno-occipitalis, nach Untersuchungen von Hermann Steiner," *Centralbl. f. allg. Path. u. path. Anat.*, 1894, **5**, 457.

SELINSKY, HERMAN. "Intracranial Chordoma," *Arch. Neur. and Psych.*, 1932, **28**, 413-16.

VIRCHOW, R. "Untersuchungen über die Entwickelung des Schädelgrundes," Berlin, 1857.

THE EFFECTS OF DIENCEPHALIC STIMULATION ON URINARY BLADDER TONUS.

BY JOHN BEATTIE AND ALAN S. KERR.[1]
(Research Laboratories, Royal College of Surgeons of England.)

Introduction.

The physiological phenomena to be described were observed in the course of a series of experiments undertaken to establish the rôle of the hypothalamus in the control of the activity of the abdominal viscera. The effects on the intravesical pressure produced by electrical stimulation of the hypothalamus were correlated with the various nuclei and tracts from which effects were obtained.

Experimental Methods.

Cats were used throughout the series. Anæsthesia was induced by chloralose injected intravenously in doses of 50 milligrammes per kilo body-weight after a preliminary ether narcosis. The animals were kept warm and left undisturbed for a period varying from thirty minutes to two hours before stimulation was attempted.

The urethra was exposed through a short suprapubic incision and a glass cannula inserted about one inch from the bladder neck and tied into position so that the upper end of the cannula projected into the bladder. The abdominal incision was then closed. As soon as the cannula filled with urine it was connected to a direct-recording water manometer previously filled with warm water. A T-piece was inserted into the rubber tube connecting the cannula to the manometer, so that the bladder could be emptied and a known quantity of fluid (usually 25 c.c.) introduced into the bladder at the beginning of the experiment. The cross-sectional area of the manometer was 0·44 sq. cm., hence a rise or fall of 10 cm. was equivalent to a change in bladder volume of 4·4 c.c. As the pressure changes often reached this figure, the experimental results recorded are changes in bladder pressure with accompanying but known small changes in bladder volume. No attempt was made to eliminate completely variations in bladder volume.

[1] Ernest Hart Memorial Scholar, British Medical Association and Thelwall Thomas Fellow of the University of Liverpool.

The head of the cat was fixed in the Souttar stereotaxic instrument so that the stimulating electrode could be introduced parallel to the line joining the external bregmatic point to the mid-point of the optic commissure. In order to eliminate as far as possible variations in the points stimulated, cats weighing between 2·5 and 3 kg. were used exclusively. It was found convenient to remove a rectangular area of bone from the top of the skull extending from 0·5 cm. in front of bregma to a distance posterior to bregma of about 3 cm. and measuring in width about 1 cm. on each side of the middle line. Bleeding was checked by bone wax, muscle implants and hot saline. Two longitudinal incisions, a few millimetres on each side of the longitudinal sinus, enabled the anterior and posterior ends of the exposed sinus to be clipped with Cushing's silver wire clips. The sinus and falx cerebri were removed between the clips. No significant changes in bladder tonus were observed during these manipulations provided the anæsthetic was satisfactory.

Bipolar stimulation was used. The electrode consisted of two fine platinum wires sealed in glass capillary tubes, the tubes being fused together after the platinum wires were fixed. The greatest diameter of the electrode was 1·4 mm. and shortest diameter 0·7 mm. The points were 0·5 mm. apart and projected the same distance from the glass capillaries. The electrode was fixed in a holder which was attached to the electrode carrier of the stereotaxic instrument. Stimulation was effected by break shocks from an induction coil, so arranged that the current strength used was just less than the minimal amount necessary to cause contractions when applied direct to an exposed muscle. The break shocks were applied at a frequency of 60 per second.

During the routine exploration the electrode was inserted at successive points in the middle line 2·5 mm. apart and at corresponding points along planes 2·0 mm. from the middle line. Our results suggest that the area of brain stimulated by the electrode did not exceed a sphere of 2 mm. diameter, as effective stimuli were usually sharply localized and effects obtained from any one point were not reproduced from points 2 or 2·5 mm. distant.

When the experiment was completed, glass rods were introduced into the brain parallel to the plane of entry of the electrode, two anterior to the most anterior and two posterior to the most posterior stimulating points and at known and equal distances from the middle line. Two rods at right angles to the plane of entry were introduced

at known distances from the middle line and in a plane at known depth from the bregmatic point. The brain was fixed with the rods in situ by injection through the aorta of 10 per cent. formalin after preliminary washing with normal Ringer or saline solution. The head was removed and immersed in 10 per cent. formalin for at least forty-eight hours.

Blocks were prepared after double impregnation with celloidin and paraffin. Sections were cut at 40 microns. In the early experiments sections were cut in the frontal plane and parallel to the plane of entry of the electrode, but in the later work a horizontal plane at right angles to the plane of entry was used. This had the advantage that all stimulated points could be seen on a single slide. The shrinkage factor was determined at 8-10 per cent.

Each alternate pair of sections was mounted so as to give two series of sections (*a*) a cell series, stained with cresyl violet, and (*b*) a fibre series, stained with Weil's iron hæmatoxylin (Weil, 1928). The tracks made by the electrodes were usually marked by areas of extravasated blood. In the fibre series a pale unstained zone surrounded the hæmorrhage at the tip of the electrode track. This zone did not measure more than 2 mm. in diameter. Such a zone was found only at the tip of the track and only when a stimulating current had been used. It may be taken, therefore, as some indication of the extent of the area stimulated.

The conventions used in indicating a specific point of stimulation indicate the distance from the bregmatic point in three planes. The zero line is the line joining the bregma to the mid-point of the optic commissure, the electrodes always being inserted parallel to this line. Point 0·25 thus indicates that the point stimulated is on the middle plane (antero-posterior) in the bregmatic line and 25 mm. below bregma, while Point 1·25 indicates a point in the middle plane 2·5 mm. posterior to bregma and at a depth of 25 mm. below the horizontal plane passing through bregma. Point 3·25·2 R. indicates a Point 7·5 mm. behind bregma in an antero-posterior plane, 25 mm. below the horizontal plane through bregma, and 2 mm. to the right of the middle plane. Thus the references to the antero-posterior plane are indicated by figures which give the distance from the bregmatic point in multiples of 2·5 mm.

Experimental Results.

Stimulation of the Posterior Hypothalamus and Upper Mid-brain.

The most striking phenomenon which we observed on stimulation of this region was a complete inhibition of bladder tonus, with cessation of

any spontaneous contractions of the organ. In Cat 29 (fig. 1) the electrode was introduced into the brain in the middle line 15 mm. behind the bregmatic point and 25 mm. below the level of bregma (Point 6·25). The mechanical stimulus caused by the introduction of the electrode produced relaxation of the bladder musculature. Electrical stimulation maintained this inhibition, but normal activity returned within one minute of the cessation of stimulation and withdrawal of the electrode.

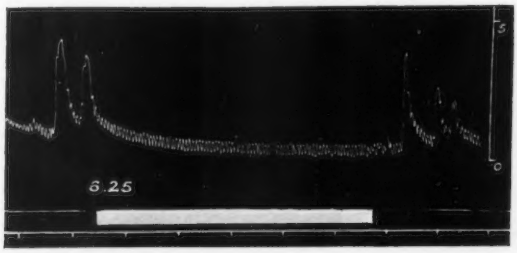

FIG. 1.—Fall in intravesical pressure and abolition of spontaneous rhythmic contractions on stimulation of the posterior and dorsal portion of the nucleus hypothalamicus posterior. Pressure in cm. of water and time marker in minutes.

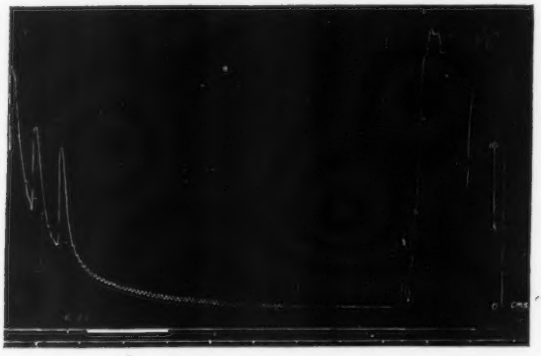

FIG. 2.—Fall in intravesical pressure and abolition of spontaneous contractions in a very "active" bladder. Note the complete absence of activity for 5½ minutes after cessation of the stimulus. The "rebound" phenomenon is well demonstrated. Pressure in cm. of water and time marker in minutes.

During the period of inhibition small waves are seen on the tracing which are synchronous with respiration and are due to transmitted pressure through the abdominal cavity.

In Cat 30 (fig. 2) the bladder was unusually active, showing large oscillations in pressure which were not synchronous with respiration.

When the electrode was introduced pressure fell rapidly, and on electrical stimulation remained low for a period of five and a half minutes after the cessation of the stimulation. Pressure returned to normal very rapidly. The point stimulated was in the middle line 15 mm. posterior to the bregma and 24 mm. below the level of this point (Point 6·24). The fall in bladder tonus on stimulation in the region of the upper mid-brain (Point 5·23) is particularly well marked in Cat 71 (fig. 4 A). It was suggested to us by Barrington that these inhibitory effects may be due entirely to the stimulation of the adreno-secretory nuclei or pathways in the hypothalamus with a consequent release of adrenalin. That adrenalin does give marked inhibition of bladder tonus can be seen in fig. 4 B (Cat 71). It was thus necessary to demonstrate whether the release of adrenalin into the circulation formed the whole or

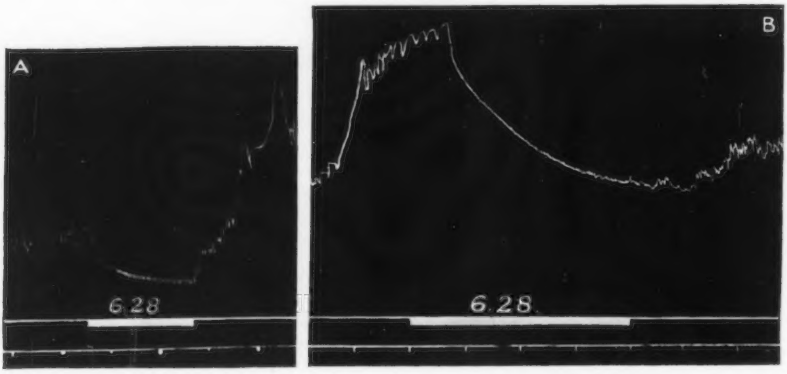

FIG. 3.—(A) Fall in intravesical pressure and abolition of spontaneous contractions on stimulation of Point 6·28, with " rebound " on cessation of stimulus. (B) After exclusion of adrenalin from the general circulation, stimulation of the same Point 6·28 is still effective.

only part of this inhibitory mechanism. Stimulation at Point 6·28 in one animal (Cat 49) gave a typical inhibition of bladder tonus with rapid recovery to normal activity on cessation of stimulation (fig. 3 A). After complete ligation of the adrenal vessels the same point was stimulated with a resulting fall in bladder tonus (fig. 3 B). Further stimulation at this point some minutes later produced an identical effect. After the animal was killed a solution of Prussian blue was forced under pressure into the inferior vena cava in an attempt to drive some of the substance into the adrenal glands, but without success.

In another animal complete inhibition of bladder tonus was obtained (fig. 4 A) by stimulation at Point 5·23. After one dose of ergotamin

(0·5 mgm.) 1 mgm. of adrenalin still produced well-marked inhibition of bladder tonus. Another 0·5 mgm. dose of ergotamin (seven minutes after the first) was administered and Point 5·23 stimulated five minutes after this injection. The effect produced was less well marked (fig. 4 B). Five minutes later 1 mgm. of adrenalin produced but little effect, and two minutes later stimulation at Point 5·23 gave a very slight fall in

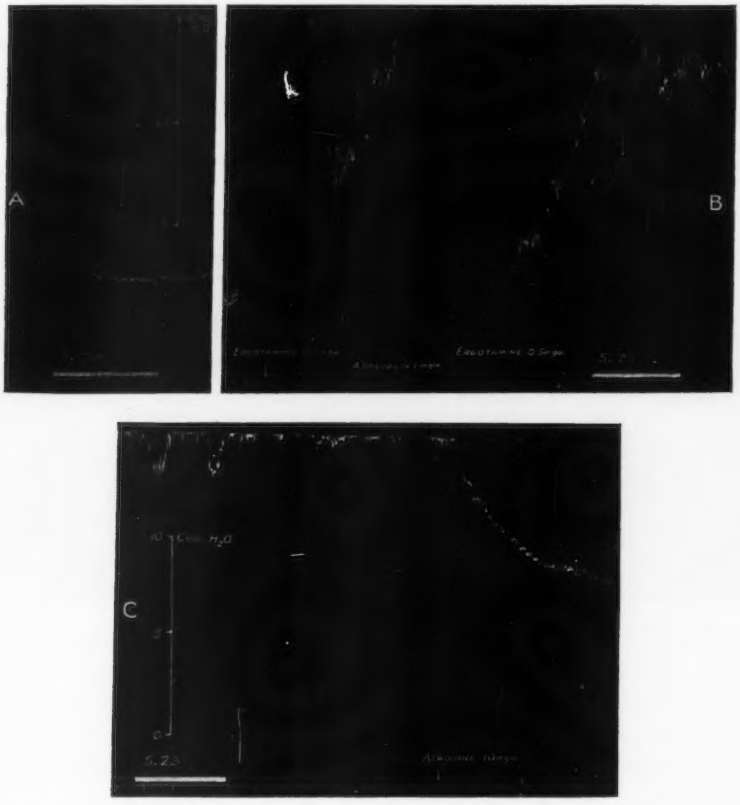

FIG. 4.—The effects on intravesical pressure of posterior hypothalamic stimulation (Point 5·23) and the modification of the response by ergotamin and atropin (see text). Time marker in minutes.

bladder pressure (fig. 4 C). After the second injection of ergotamin it was noted that the bladder pressure rose steadily reaching 15 cm. H_2O, beyond which it was not possible to record it. After stimulation at Point 5·23 for the third time, 10 mgm. of atropin injected intra-

venously produced a steady decline in bladder pressure which eventually reached almost zero level (fig. 4 c). It would seem, therefore, that the region stimulated in these experiments contains not only adreno-secretory fibres and cells, but also fibres and cells which can influence the bladder directly, producing in that organ the typical sympathetic effect—relaxation.

Stimulation of the Anterior Region of the Hypothalamus.

The phenomena which we observed during stimulation in this area were essentially the reverse of those recorded for the posterior hypothalamus, that is, there was a rise in bladder pressure during stimulation with some increase in the height of the spontaneous bladder contractions in some experiments. Of these two effects the former was much more constant. The type of response obtained from stimulations in this

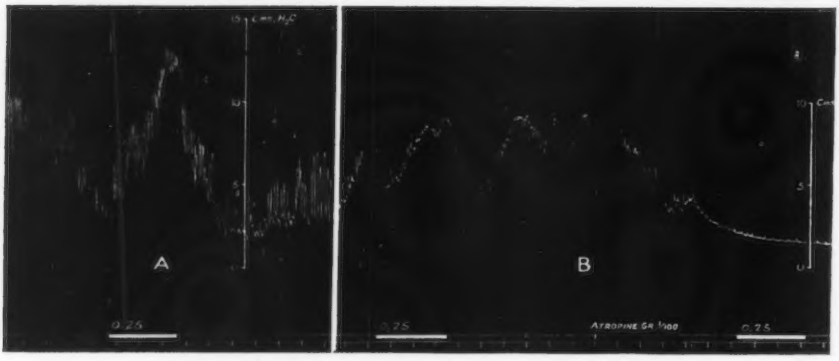

FIG. 5.—The effect of anterior hypothalamic stimulation (Point 0·25), showing increase in bladder tonus and abolition of the effect after atropinization. Time in minutes.

region depended to a great extent on the state of activity of the bladder before stimulation was applied. When the bladder displayed little or no spontaneous contractions the result of stimulation was an increase in intravesical pressure, but when the bladder was active and showed great oscillations in pressure the tonic effect was masked to some extent by these oscillations. Fig. 5 A shows an animal with a moderately active bladder responding to a stimulus in the anterior hypothalamus (Point 0·25) by a marked rise in tonus with little or no effect on the spontaneous contractions. The same animal showed at a later stage of the experiment a very decided diminution in the contractions, but the tonic effect was equally well marked on stimulation of the same point.

The activity of this bladder was remarkable, as there was a spontaneous rhythmic variation in the intravesical tension which occupied fully four minutes to complete a cycle. The pressure climbed by a series of well-marked contractions to a maximal point, and then declined relatively rapidly. During the decline the spontaneous contractions were absent. On stimulation of the anterior hypothalamus (Point 0·25) during the period of decline, the tonic effect was produced, but on cessation of the

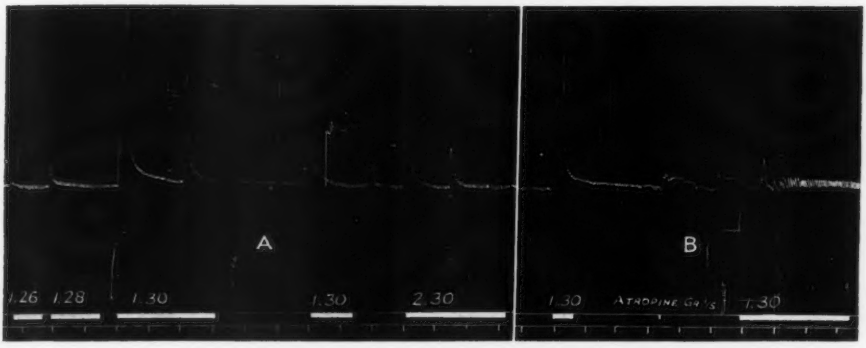

FIG. 6.—Rises in intravesical pressure from stimulation points in the tuber cinereum and upper mid-brain (Points 1·30 and 2·30). Abolition of the effect by atropin. Time marker in minutes.

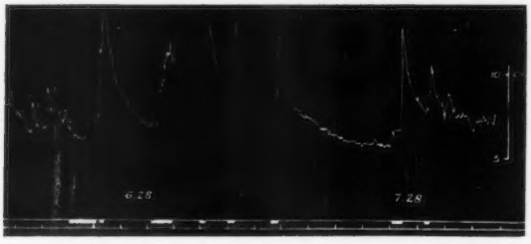

FIG. 7.—Rises in intravesical pressure on repeated stimulations at Points 6·28 and 7·28 (block signals) lying close together in the white matter on the dorsal surface of the grey matter of the aqueduct at the level of the inferior colliculi. Pressure in cm. water. Time marker in minutes.

stimulus the pressure fell rapidly and the cycle of rise and fall in tension commenced again (fig. 5 B). The injection of atropin abolished not only the intravesical pressure but also the spontaneous contractions of the organ. Stimulation of the point (0·25) mentioned previously, did not produce the pressor effect, nor did the stimulation of a point (4·25) which had previously caused a fall in bladder tonus produce any further

ABBREVIATIONS FOR PLATE FIGURES.

A. = Aqueduct of Sylvius.
C.I.C = Commissure of the inferior colliculus.
F. = Fornix.
I.C. = Inferior colliculus.
I.P.S. = Inter-peduncular space
I.R. = Infundibular recess.
M.B. = Mammillary body.
M.T.T. = Mammillo-thalamic tract (Vicq d'Azyr).
N.E.W. = Nucleus Edinger-Westphal.
N.R. = Nucleus rubra.
N.T.C. = Nuclei of posterior tuber cinereum.
P.C. = Posterior commissure.
T.P.T. = Thalamo-peduncular tract.
V. III = Third ventricle.

Points 0·25, 1·30, &c. = corresponding stimulating points in text-figures.

PLATE.

FIG. 1.—Section cut in frontal plane showing tip of electrode track at the periphery of the grey matter on the floor of the aqueduct. Stimulation of this point produced a fall in intravesical pressure. × 10.

FIG. 2.—Horizontal section through dorsal region of diencephalon to show stimulation point (5·23) of text-figure 4. × 10.

FIG. 3.—Horizontal section to show stimulation point (6·28) of text-figure 3. Point lies close to ventral surface of aqueduct grey matter. × 10.

FIG. 4.—Horizontal section to show stimulation point (0·25) of text-figure 5. Point lies in periventricular fibre system. × 10.

FIG. 5.—Horizontal section through tuber cinereum and mammillary bodies to show stimulation point (1·30) of text-figure 6. Point lies amongst the fibres of supra-mammillary decussation. × 10.

FIG. 6.—Horizontal section through dorsal region of mid-brain. Stimulation points (6·28 and 7·28) lie amongst the longitudinal fibres on the ventral surface of the decussation of the inferior colliculi (text-fig. 7). × 10.

PLATE III.

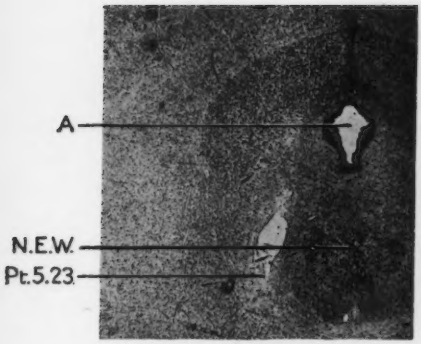

FIG. 1

FIG. 2

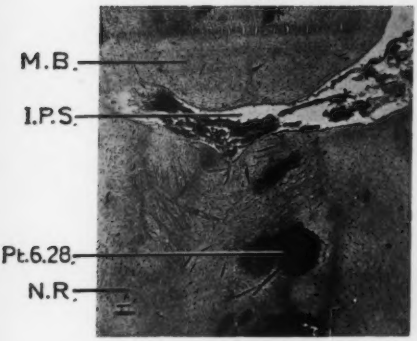

FIG. 3

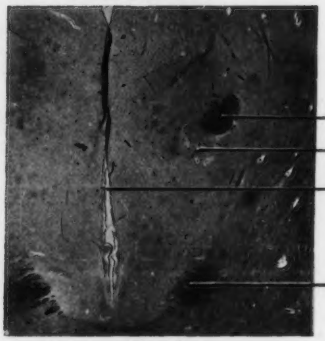

FIG. 4

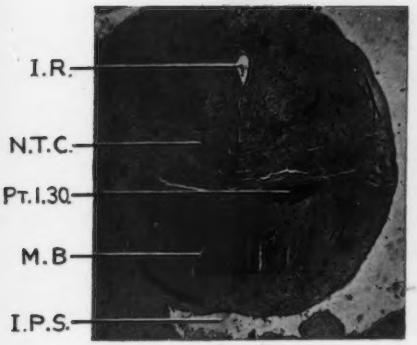

FIG. 5

FIG. 6

To illustrate paper by John Beattie and Alan S. Kerr.

decline in bladder pressure when stimulated. The effective pressor area is apparently well circumscribed. Stimulation of adjacent points distant from it two millimetres or more gave no response, except along a well-defined tract running posteriorly.

Tracing 6 A from Cat 69 shows the effect of stimulation of the posterior part of the tuber cinereum (1·30) and of a point 2·5 mm posterior to 1·30 on a hitherto inactive bladder. There is a sharp rise in tonus which is not maintained throughout the period of stimulation. This effect was twice repeated, but after the injection of 12·5 mgm. of atropin, further stimulation was almost wholly ineffective (fig. 6 B). Cat 54 (fig. 7) shows the effect of stimulation of the dorsal part of the lower mid-brain. It again reveals very sharp rises of tonus maintained for a short time at micturition level, but falling rapidly as soon as stimulation ceases. We regarded these effects as being due probably to the stimulation of fibre pathways passing from the anterior hypothalamic region posteriorly into the brain-stem.

Histological Localization of Effective Stimulation Points.

In the previous section the effects of stimulation were discussed in terms of linear co-ordinates measured along three reference planes at right angles; it is necessary, therefore, to correlate these various effective stimulation points with various nuclei and tracts of the hypothalamus.

All the points which on stimulation gave rise to a diminution of intravesical pressure lay behind the level of the pituitary stalk, i.e. in the posterior part of the hypothalamus. More precisely these effective points were related to the nucleus hypothalamicus posterior or its backward continuation into the ventral part of the grey matter of the sylvian aqueduct. The most effective stimulation points were found to lie in the periphery of the grey matter of the floor of the aqueduct just caudal to its junction with the third ventricle. The reason for this is obvious when one remembers the widely scattered cells of the nucleus hypothalamicus posterior, and the concentration of the projection tracts from this nucleus into the peripheral region of the floor and lateral wall of the aqueduct.

The first two figures on Plate III indicate the anatomical relation of the efferent sympathetic tracts to the aqueduct. Plate III, fig. 3 is of interest, as the effective stimulation point is almost exactly in the middle line and has stimulated the fibre tracts which lie on the periphery of the grey matter of the aqueduct floor (see text-figs. 3 A and 3 B).

The experiments which have been described above leave no room for

doubt that fibres related directly to the bladder in addition to adrenalo-secretory fibres are present in this region. In the same region, too, are the fibres which Beattie, Brow and Long (1930) showed to be related to the sympathetic control of the heart.

Increased intravesical pressure and increased rhythmic bladder contractions were obtained from a much more anterior region. Again, the most striking results on bladder tonus were obtained from regions where there is a considerable concentration of fibre tracts and not from the diffuse nuclear masses.

Plate III, fig. 4, demonstrates an effective stimulation point (text-fig. 5) just caudal to and slightly internal to the fornix bundle. Examination of the sections stained for fibres shows that this point lies in the periventricular fibre system. As the fibres of this system pass posteriorly some swing medially and cross the middle line in the supra-mammillary decussation. Stimulation of these decussating fibres also produces an increase in bladder pressure. (Plate III, fig. 5 and text-fig. 6 A and B.) The histological sections demonstrate that the fibre tracts are passing between the nuclei tuberis and the upper poles of the mammillary bodies. More posteriorly the fibre tracts have been shown to lie in the dorsal part of the periphery of the grey matter of the aqueduct (Plate III, fig. 6 and text-fig. 7). In the section shown the fibre tracts are stimulated as they lie anterior to the commissure of the inferior colliculus.

Our experiments do not indicate precisely which of the anterior hypothalamic nuclei can be regarded as the site of origin of these fibre tracts. One of the cell masses in the supra-optic or pre-optic areas may be concerned, but the presence in these regions of numerous fibres of passage does not allow us to regard effects obtained from them as "nuclear" rather than "tract" effects.

Discussion.

Since the classical experiments of Elliot (1907) in which he established the double innervation of the urinary bladder, many workers have tried to distinguish the exact functions of the nerves. Regarding the fundus of the bladder, opinion as a whole is agreed that the pelvic nerves are motor to the detrusor muscle while the hypogastric nerves inhibit. The internal sphincter of the bladder has the hypogastric nerve as its motor supply, while the pelvic nerves are inhibitory. Henderson and Roepke (1934) have recorded an increase in intravesical pressure following the injection of acetylcholine. This effect is not produced if a previous injection of atropin is administered. This finding is in

opposition to the view of Macdonald and M'Crea (1930) that drugs having either parasympathetic or sympathetic pharmacological actions may give rise equally to motor or inhibitor effects.

In this paper we are dealing only with the control of bladder tonus and not with the mechanism of micturition. In Barrington's (1921, 1925, 1927, 1933) work on the control of micturition he has recognized five centres for the control of this reflex act, two of which lie in the brain-stem. Only one of his experiments suggests a level of control above the upper pons in the cat. Langworthy and Kolb (1933) found that transection of the mid-brain at the level of the anterior part of the superior colliculi did in some way interfere with the intravesical pressure, for they found that in such animals the amount of water required to be introduced into the bladder, to raise its internal pressure to that level necessary to produce micturition, was much less than normal. This would suggest that, above the level of the transection, there is some mechanism for the inhibition of the smooth muscle of the bladder.

In our experiments the results suggest that there is not only a mechanism for the inhibition of bladder tonus, but also an additional one which can increase the bladder tonus much above the normal level. The histological findings lead us to believe that the former reaction is obtained from the posterior hypothalamic nuclei and their projection tracts which surround the floor and lateral wall of the grey matter of the aqueduct. In the case of the latter reaction the pressor effect is obtained from the more anterior hypothalamus, the nuclei concerned being probably in the supra-optic or pre-optic areas. Where the pressor effects were obtained from stimulation of the posterior hypothalamus and dorsal part of the aqueduct fibre system, it seems logical to suggest that these are due to stimulation of efferent pathways from more anterior nuclei passing through these regions.

Conclusions.

(1) The effects of controlled and histologically localized electrical stimulation of the hypothalamus and upper mid-brain on the tonus and activity of the urinary bladder are described.

(2) Evidence of the existence of centres for the increase of tonus in the anterior hypothalamus and for inhibition of tonus in the posterior hypothalamus and upper mid-brain is adduced.

(3) Bladder inhibition, due to hypothalamic stimulation, is produced

by the activation of direct nervous pathways to that organ, and also by the stimulation of adrenalo-secretory fibres.

(4) The striking responses obtained by stimulation of the mid-brain are explained as being due to activation of effector pathways in the white matter on the periphery of the central grey matter of the aqueduct of Sylvius.

We wish to express our thanks to Mr. S. P. Steward and the technical staff of the Royal College of Surgeons for their assistance at all stages of the work.

REFERENCES.

BARRINGTON, F. J. F. *Brain*, 1921, **44**, 23.
Idem. *Quart. Journ. Exper. Physiol.*, 1925, **15**, 81.
Idem. *Proc. Roy. Soc. Med.*, 1927, **20**, 722.
Idem. *Brain*, 1933, **56**, 126.
BEATTIE, J., BROW, G. R., and LONG, C. N. H. *Proc. Roy. Soc.*, Series B, 1930, **106**, 253.
BEATTIE, J., and SHEEHAN, D. *Journ. Physiol.*, 1934, **81**, 218.
CLOAKE, P. C., LEARMONTH, J. R. and BARRINGTON, F. J. F. *Proc. Roy. Soc. Med.*, 1932, **25**, 547.
ELLIOTT, T. R. *Journ. Physiol.*, 1907, **35**, 367.
HENDERSON, V. E., and ROEPKE, M. H. *Journ. Pharmacol. and Exper. Therap.*, 1934, **51**, 97.
INGRAM, W. R., HANNETT, F. I., and RANSON, S. W. *Journ. Compt. Neurol.*, 1932, **55**, 333.
KABAT, H., MAGOUN, H. W., and RANSON, S. W. *Arch. Neurol. and Psych.*, 1935, **34**, 931.
LANGWORTHY, O. R., and KOLB, E. *Brain*, 1933, **56**, 371.
LANGWORTHY, O. R., REEVES, D. L., and TAUBER, E. S. *Ibid*, 1934, **57**, 266.
LEARMONTH, J. R. *Ibid.*, 1931, **54**, 147.
MACDONALD, A. D., and M'CREA, E. D'A. *Quart Journ. Exper. Physiol.*, 1930, **20**, 379.
RIOCH, D. McK. *Journ. Compar. Neurol.*, 1929, **49**, 1, 121.
Idem. *Ibid.*, 1931, **53**, 319.
WEIL, A. *Arch. Neurol. and Psych.*, 1928, **20**, 392.

FURTHER OBSERVATIONS UPON GRASPING MOVEMENTS AND REFLEX TONIC GRASPING.

BY F. M. R. WALSHE AND J. H. HUNT.

Psychological and Reflex Factors in the Production of Grasping Phenomena.
The Influence of Apraxia and Hypertonus.
Relationship between Grasping Phenomena and the Righting Reflexes of Magnus and de Kleijn.
Summary.
References.

Psychological and Reflex Factors in the Production of Grasping Phenomena.

Observations recorded in this journal [7] by Walshe and Robertson led them to conclude that in the complex of phenomena known as "forced grasping" there are two distinct and separable components. These are (i) *volitional grasping movements* in response to objects seen, or to contacts felt in the palm of the hand, and (ii) *reflex tonic grasping* in response to stretching of the flexor muscles of the fingers.

The physiological significance of each of these components was discussed in the paper in question.

A further series of cases has since been investigated by the present writers with a view to studying separately the visual, tactile and proprioceptive factors in stimulation. For this purpose use was made of the method of blocking the cutaneous nerves to the hand, median, ulnar and radial, with novocain. The hand was thus rendered anæsthetic and the tactile factor eliminated. If, in addition, the patient was blindfolded, vision was also excluded and the factor of stretch could be observed in isolated operation.

The modifications introduced into the grasping phenomena by the presence of apraxia and of hypertonus in the affected limb have also been considered. In one case, also, it was possible to elicit from the patient useful information as to the mental factors which in him determined the occurrence of grasping.

Case 1.—F. A., a man aged 47. (National Hospital, 1935.)

History.—Subject for three months to Jacksonian attacks involving the right

hand and leg. No loss of consciousness. For a month a slowly progressive right hemiparesis had been developing. It had become difficult for him to concentrate his attention, and he was said to have become a little "simple" in the past few weeks.

General examination.—Fully conscious and co-operative. Attention not normally sustained. Speech normal. Bilateral papillœdema (2D, right and left). Slight weakness of left external rectus with diplopia to left. Slight paresis of right lower face. Tongue protruded straight.

Slight right-sided hemiparesis with just appreciable hypertonus in the flexors of the upper and the extensors of the lower limb. The range of unresisted movement is full. In the hand there is slight weakness of grasp and a trace of clumsiness of finger movements. All forms of sensation are normal. The tendon jerks are brisker on the right than on the left, the right abdominal reflexes are diminished, but both plantar responses are of normal flexor type.

(i) *The patient's account of his grasping movements.*—During the various examinations of this man, his own comments upon the grasping propensities of his right hand were of considerable interest. He said: "I can't leave things alone. If I see anything lying near me, my hand seems to want it. At meal time my hand butts in and picks up things I don't want." "If I happen to look at something my hand seems to want it." "If I'm standing near a door I can't help catching hold of the handle, even if I know I don't want to open it, but just if the idea of opening it comes to me." "My hand—and not me—seems to want it."

(ii) *Examination of grasping movements.* — During one conversation a cigarette was laid upon the bed near his right hand, the patient sitting up in bed at the time. Every twenty or thirty seconds the right hand stole out towards the cigarette. Sometimes it was grasped, but at other times he suddenly seemed to notice what was happening and checked the right hand. Sometimes he seemed to find it easier to stretch out the normal left hand with which he grasped the right and pulled it back. This process was repeated many times. A wisp of cotton-wool was then substituted for the cigarette. After two grasping movements, the process stopped and in a few seconds the patient said, laughing, "My hand doesn't want it now." The cigarette was then replaced, and the process resumed with its original persistence. It appeared that the attractiveness of the object seen determined in a measure its potency as a stimulus to grasping movements.

His hand closes gently round the observer's fingers when these are introduced into his palm, and much more completely and rapidly when they are introduced between thumb and index than when they are introduced from the ulnar side.

He is able to relax a voluntary grasp (clenching) without difficulty, though not quite so rapidly as with the left (normal) hand, and this whether the hand be empty or whether it contains such an object as a fountain pen, or wooden rod. It may be noted that all movements of the right upper limb are slightly

slower than those of the left, a fact which may be correlated with the slight paresis and hypertonus.

During the systematic testing of sensation on the palmar surface of hand and digits, no grasping movements were observed.

(iii) *Examination of reflex tonic grasping.*—No tonic grasping was observed unless the fingers were passively extended and stretch put upon the flexor muscles. In these circumstances typical tonic grasping ensued, but this could be relaxed by the patient on request, slowly and with apparent effort.

(iv) *Median nerve blocking.*—Two per cent. novocain solution was injected into the median nerve one inch proximal to the wrist line. Complete cutaneous anæsthesia and analgesia was obtained over the median nerve area.

Grasping movements.—When observer's fingers are introduced into the palm, the patient's eyes being blindfolded, no grasping movement is seen until the finger tips reach the area of normal sensation on the ulnar side of the palm. If they be introduced from the ulnar side there is some flexion of the fingers, most marked of the little and ring fingers. If the patient be allowed to look at his hand during this procedure, grasping movements ensue even when contact is confined to the anæsthetic area of the palm.

Reflex tonic grasp.—This is wholly unimpaired in intensity despite the insensitiveness of the skin of the hand. Using a spring balance with an attached loop which was passed round the flexed fingers singly, the following tensions were obtained before the finger was pulled out straight. Index. 20 lb.; middle finger, 15 lb.; ring finger 15 lb.; and little finger 14 lb.

(v) *Median, ulnar and radial nerve blocking.*—On a subsequent occasion both median and ulnar nerves were blocked above the wrist, and the radial nerve in the lower third of the forearm with 2 per cent. novocain solution. The hand became completely anæsthetic to touch, pin-prick, heat and cold to a line about one inch proximal to the wrist. *With the patient's eyes open* grasping movements occurred when the palmar aspect of hand or fingers was touched by the observer's fingers, and also when a cigarette was placed on his palm. With the patient's eyes covered no trace of grasping movement ensued when passive extension of the fingers was eliminated by placing the hand palm upwards upon a plaster cast made to the dorsum of the hand. In these circumstances, touch and pressure were without effect.

Reflex tonic grasp.—As in the previous observation, the response to stretch of the finger flexors remained wholly unimpaired in intensity, and it was clear that stretch was the sole operating stimulus.

All the familiar features of grasping movements and of reflex tonic grasping as recorded by Walshe and Robertson are exemplified in this case. The primacy of psychological factors in the causation of the grasping movements is particularly well illustrated. An object seen acts as a stimulus in respect of the ideas with which it has come to be associated in the patient's mind, and in respect of the emotional tone accompanying these ideas. A stimulus is adequate in respect of

its place in the individual experience of the patient. Thus, a cigarette has become a more desirable object than a wisp of cotton-wool and for this reason, and this reason alone, acts as a more potent stimulus to grasping movement.

The decisive role of psychological factors in determining the adequacy of tactile stimuli to elicit grasping movements was apparent in the observations already referred to (7).

Fulton still maintains [3] that these volitional movements are as wholly reflex as the invariable tonic grasping which persists even in the unconscious patient. He does this in virtue of a belief that "the one fundamental tenet in the creed of modern neurophysiology" is the reflex nature of all possible movements. Tenets and creeds belong to other disciplines than that of science, and in fact this objection was fully discussed by Walshe and Robertson. Arguing upon the same lines as these writers, Creed [2] has recently put the position quite clearly; thus: "To many it would seem advisable to confine the use of so well-established a technical term as 'reflex' to the concept for which Marshall Hall in 1833 introduced it into the vocabulary of science, namely, to describe responses dependent upon inherited structure in the nervous system and not on individual experience. Hall considered that 'the excited motions which belong to the reflex function are independent of sensation.' Unless it can be proved that consciousness is an ineffective bye-product of central nervous activity, it is probably wise for us to exclude from the category of reflex action all phenomena in which mental activities may play an essential part." We may therefore continue, without fear of physiological heresy, to regard the movements in question as volitional, though probably of the kind that Jackson would have called "least voluntary, most automatic."

This case also exemplifies the fact that reflex tonic grasping has as its sole adequate stimulus stretch of the flexor muscles of the fingers, and persists unimpaired when both visual and tactile stimuli have been eliminated. It is a proprioceptive reaction, completely independent of volition or of any mental activity.

The use of nerve blocking of the cutaneous supply of the hand was adopted in a second similar case, and with results identical with those described above.

The Influence of Apraxia and of Hypertonus.

It was emphasized by Walshe and Robertson that the subject of "forced grasping" could open his clenched fist easily when it was empty and even when it contained an object which was not being pulled away

so as to stretch the flexors of the fingers. Occasionally a case may be seen in which the subject appears to have more or less difficulty in relaxing the grasp of his empty hand. This apparent exception to the general rule does not necessitate any revision of our view as to the cause of tonic grasping, and it is, in our experience, always due to the intervention of other factors. Apraxia is perhaps the most important of these, and the patient's inability to open his empty fist on request in a case of reflex tonic grasping is commonly due to apraxia. The following case illustrates this.

Case 2.—*Glioma in right parietal lobe. Voluntary grasping movements, reflex tonic grasping and apraxia of left hand.*

H. A., a man aged 48. (National Hospital, 1935.)

History.—Two months history of Jacksonian attacks of the left arm, with progressive hemiparesis of the left side.

General examination.—Fully conscious, but fatuous. Attention ill-sustained. No papillœdema. Slight left hemiparesis with just appreciable hypertonus of the limbs, tendon jerks increased in left limbs, abdominal reflexes present on both sides, both plantar responses flexor. Left hemi-hypæsthesia to touch, pinprick, heat and cold, postural sense.

A right subtemporal decompression revealed a glioma (astrocytoma) in the right parietal region.

Tests for Apraxia.

Face.—Could carry out the following movements in order correctly and without error or delay: Put out tongue; Shut eyes; Show teeth; Shake head; Nod; Whistle.

	R.	*L.*
Arms.—Beckon.	Correct.	Says, "It won't come up," then extends index finger and says, "It won't move."
Shake fist.	Correct.	Clenches fist, then opens hand and looks at it. Says, "It won't come up."
Shake hands.	Correct.	Lifts hand to shake.
Open hand.	Correct.	No movement—then after a long pause opens it easily.
Touch thumb and little finger.	Correct.	Extends and abducts all digits and looks at them.
Finger to nose.	Correct.	Clenches fist, then opens it. Says, "It won't come up."
Brush hair with brush.	Correct.	Holds brush, does nothing. Says, "I can't get the brush up, it beats me."

	R.	*L.*
Strike a match on box.	Correct.	Opens box with right hand, takes out match with left and holds it against the side of the box without striking it. When it is struck for him, he blows it out spontaneously.
Put on glasses.	Correct.	Holds glasses and fumbles. Does not put them on nose.
Comb moustache.	Correct.	Holds comb and looks at it helplessly.
Clench fist.	Correct.	Makes a grasp, but cannot be induced to squeeze the dynamometer.

He was requested to make this last movement with the left hand a number of times on different occasions. The result was variable. At times a normally rapid opening was seen. At others he looked at the hand and was unable to relax the grasp, doing so easily a few seconds later when his attention was diverted to something else. This uncertainty of response obtained whether the closed hand was empty or contained an object, such as a roll of bandage or a pencil.

Grasping movements of the left hand showed the usual features. Thus, in systematic sensory testing of the hand no grasping movements occurred. There were grasping movements when the observer's hand was approached close to the patient's in the attitude of inviting to a handshake. Stroking of the patient's palm with the observer's fingers introduced between thumb and index also elicited rapid grasping movements.

Reflex tonic grasping in response to stretch was also present. The presence of apraxia had no influence upon this.

In two other similar cases in which apraxia co-existed with grasping movements and reflex tonic grasping in the same hand, this same uncertainty of response in opening, at request, the closed hand was also seen.

Perhaps less striking is the influence of hypertonus of the grasping limb. In the spastic arm of any case of residual hemiplegia voluntary movements are notably slow, and when voluntary extension of the fingers is possible it is a slow and laboured accomplishment. Similarly, if any degree of spasticity invades the limb which shows grasping movements, there is an increased delay in the voluntary relaxation of the clenched and empty fist, but this is a function of spasticity and impaired power of movement and not of the grasping movement itself.

Occasionally, indeed, in a very spastic residual hemiplegia in which there is no trace of grasping *movements* of the kind under consideration, namely the so-called "forced grasping," the permanent hypertonus of the flexors of the fingers may be felt to be appreciably increased by

sudden passive extension of the fingers. This was well seen in the following case of old infantile hemiplegia.

Case 3.—*Infantile left hemiplegia. No grasping movements, but increased flexion of fingers in response to stretch.*

G. H., aged 17. (National Hospital, 1935.)

History.—Difficult labour. Began to walk when in third year. Fell unconscious (? epileptiform fit) when aged 10 years. Since this the left limbs have become very stiff and useless.

General examination.—Intelligent. Severe spastic left hemiplegia. The left arm is adducted, slightly flexed at the elbow, semipronated, all digits flexed except the thumb. Movements of the limb as a whole are slow, coarsely tremulous and limited in range. Voluntary grasp retains fair power.

The left leg is rigidly extended, with the foot inverted and plantar flexed. No voluntary dorsiflexion of foot.

Left tendon jerks very brisk, right normal. Left plantar response equivocal, right flexor.

Left hand and arm.—On request the flexed finger can be slowly extended, the movement taking three seconds to complete.

When the observer's hand is insinuated in the palm, there is no trace of closure round it, and no active grasping movement can be evoked by any kind of visual or tactile stimulus.

If the observer's index finger be curled under the semiflexed digits, and these are gently lifted (i.e. extended) a moderate degree of hypertonus can be felt, but if this extension be brusquely increased and sustained, then the hypertonus of the flexor muscles can be felt to increase notably and the flexed fingers retain the observer's finger—or a wooden rod—against considerable extending force.

This increased flexor tonus is undoubtedly a response to stretch, and as such is presumably allied to the reflex tonic grasping we have been considering. But the latter may be fully developed and powerful in the absence of any resting hypertonus in the affected muscles and cannot therefore be regarded simply as an expression of hypertonus.

Relationship between the Grasping Phenomena (Movements and Tonic Grasp) and the Righting Reflexes of Magnus and de Kleijn.

Fulton [3] and Bieber and Fulton [1] report that after bilateral excision of Areas 4 and 6 in the monkey, the forced grasping shown by the animal varies with the animal's position in space. With the animal supine the extremities become extended and forced grasping becomes minimal or disappears. In the left lateral position only the right

extremities exhibit grasping, and this can be inhibited by exerting pressure from above (Magnus's " Brettversuch.")

In their case of "syndrome of the premotor cortex in man" [4] which has been discussed by one of the present writers elsewhere [6] Kennard, Viets and Fulton report that in the human subject also the strength of the grasping phenomena varies with variations of the patient's position in space exactly as described above for the monkey.

From this they conclude that "the grasp is part of the righting reflex mechanism peculiar to primates" [3].

But even if these observations be confirmed, the conclusion drawn from them by Fulton does not follow, and it would be more accurate to say that grasping and the righting reflexes interact. Such interaction between reflexes of different physiological category is known to occur, and the influence of the tonic neck reflex upon the Babinski response as recorded by Walshe [5] is a case in point. We do not say, however, that the Babinski response is therefore part of the tonic reflex mechanism. Indeed, we know it is not.

Therefore indications of interaction between grasping and righting reflexes leave the existence of a relationship between them, and the possible nature of such a relationship, entirely open questions, and do not provide evidence of their identity. Indeed, so widely separate in their nature are grasping movements and reflex tonic grasping that it is difficult to see how both can be part of the same mechanism.

As to the fact of this interaction in man, no trace of influence of body posture in relation to space, or of head posture in relation to the trunk, upon either grasping movements or upon reflex tonic grasping could be found in any of our cases. We have thus been unable to confirm Fulton's observations.

SUMMARY.

Evidence is adduced to show that of the two components of "forced grasping" described by Walshe and Robertson: namely, voluntary grasping movements, and reflex tonic grasping, the former is determined by mental factors and cannot properly be called reflex, while the latter is exclusively a proprioceptive reflex reaction to stretch.

No evidence was obtained of any interaction between either of these components and the righting reflex mechanism of Magnus and de Kleijn.

Our thanks are due to those members of the Honorary Staff of

the National Hospital who have allowed us to examine and record their cases.

REFERENCES.

[1] Bieber, I., and Fulton, J. F. *Amer. Journ. Physiol.*, 1935, **105**, 7.
[2] Creed, R. S. *Nature*, 1934, **134**, 792.
[3] Fulton, J. F. *Arch. Neurol. and Psychiatr.*, 1934, **31**, 221.
[4] Kennard, M. A., Viets, H. R., and Fulton, J. F. *Brain*, 1932, **57**, 69.
[5] Walshe, F. M. R. *Ibid.*, 1923, **46**, 281.
[6] *Idem. Ibid.*, 1935, **58**, 49.
[7] Walshe, F. M. R., and Robertson, E. G. *Ibid.*, 1933, **56**, 40.

THE EFFECT OF PROLONGED OCCLUSION OF THE EXTERNAL JUGULAR VEINS ON THE CEREBRO-SPINAL FLUID AND THE TORCULAR VENOUS PRESSURES OF THE DOG.

BY T. H. B. BEDFORD.

(From the Department of Pharmacology, Manchester University.)

In an earlier paper [3] an account has been given of a number of experiments which were undertaken in order to study the effect of occlusion of the external jugular veins on the pressure of the cerebrospinal fluid and on the venous pressure in the torcular. It was found as a result of these experiments that the rise in the pressure of the cerebrospinal fluid which follows sudden occlusion of the external jugular veins is a temporary phenomenon, and that the pressure usually returns to the region of its original level within the space of one hour. The venous pressure in the torcular was also observed to fall, but the fall was not so rapid or so complete as the fall in the pressure of the cerebrospinal fluid, and at the end of the experiment the torcular venous pressure was sometimes more than twice its original height. These pressure changes were found to occur independently of variation in the systemic arterial pressure. The average duration of the experiments was two hours.

It was concluded that the fall in the pressure of the cerebrospinal fluid was due mainly to the formation of collateral venous circulation; it was also considered that there had probably been a reduction in the total volume of the cerebrospinal fluid. The experiments were conducted on fully anæsthetized and consequently immobile animals. The anæsthetic employed in these experiments was ether. The question naturally arises as to whether similar pressure levels would be found in active unanæsthetized animals. The following experiments were undertaken in an attempt to obtain information on this problem.

Before proceeding to a description of the experiments, it is necessary first to describe the precise point at which the external jugular veins were occluded. It was the custom to shave the necks of the animals in order to render visible the superficial veins. The vessels were occluded by ligation with catgut. The ligature was placed immediately below the level at which the external jugular vein receives its last tributary

from the head. This point is usually situated on a level with the body of the fourth cervical vertebra. It is important to bear in mind that an occlusion of the vein at this point obstructs not only the blood which leaves the cranium through the post-glenoid foramen, but also a considerable amount of the blood from the muscles and soft parts of the head. Owing, however, to the great variations in the mode of termination of the tributaries of the external jugular veins which were encountered in different animals, it was felt that a more uniform degree of venous congestion could perhaps be obtained by ligating at this site than by attempting to occlude the vein at a higher level in the neck. For details of the intracranial venous system of the dog, reference should be made to previous publications [2, 3].

At an early stage in the investigation the external jugular veins were occluded in five dogs. The animals were allowed to survive for varying periods up to six weeks when they were killed. During post-operative life the animals appeared normal in all respects. A careful examination of the brains after death failed to reveal any evidence of hydrocephalus or of other abnormalities. It was also noted that the intracranial venous sinuses were free from clot and that the external jugular veins were patent close up to the ligatures. The internal jugular veins were found to be considerably dilated. It was evident from these experiments that occlusion of the external jugular veins does not cause hydrocephalus in dogs when the animals are observed for periods up to six weeks.

An attempt was now made to record the cerebrospinal fluid pressure and the torcular venous pressure in animals in which the external jugular veins had been occluded twenty-four hours previously. The experiments were conducted as follows: The dogs were anæsthetized with ether and the external jugular veins ligated at the site already indicated. They were then allowed to recover

TABLE I.

Dog No.	Cerebrospinal fluid	Torcular venous	Femoral artery
1	240	190	130
2	240	220	125
3	270	260	125
4	210	265	130
5	205	225	125

The cerebrospinal fluid pressure, the torcular venous pressure and the arterial pressure in the femoral artery in five dogs in which the external jugular veins had been occluded twenty-four hours previously. The pressure of the cerebrospinal fluid and the torcular venous pressure are recorded in millimetres of normal saline solution, the pressure in the femoral artery in millimetres of mercury.

from the anæsthetic and twenty-four hours later they were again anæsthetized and a simultaneous reading taken of the following pressures: (*a*) the cerebrospinal fluid pressure in the cisterna magna; (*b*) the venous pressure in the torcular; (*c*) the systemic blood-pressure in the femoral artery. The results of five experiments are contained in Table I. It will be observed that these readings show a close similarity to those obtained immediately after the external jugular veins had been occluded (Table II). These latter figures are extracted from an earlier publication [3].

TABLE II.

Dog No.	Cerebrospinal fluid	Torcular venous	Femoral artery
1	210	195	110
2	230	210	115
3	255	270	90
4	230	280	130
5	200	195	120

The cerebrospinal fluid pressure, the torcular venous pressure and the arterial pressure in the femoral artery in five dogs immediately after occlusion of the external jugular veins. The pressure of the cerebrospinal fluid and the torcular venous pressure are recorded in millimetres of normal saline solution, that in the femoral artery in millimetres of mercury.

The intracranial pressures were now recorded in animals in which the external jugular veins had been occluded for periods longer than twenty-four hours. High pressures were observed up to the third or fourth day, but after a week the cerebrospinal fluid pressure was generally normal while the venous pressure, although considerably reduced, was usually above its normal level. The pressure readings in four animals in which the external jugular veins had been occluded seven days previously are indicated in Table III. These findings were most unexpected. Experiments of two to three hours' duration on

TABLE III.

Dog No.	Cerebrospinal fluid	Torcular venous	Femoral artery
1	135	155	115
2	120	160	120
3	150	200	125
4	195	180	120

The cerebrospinal fluid pressure, the torcular venous pressure and the arterial pressure in the femoral artery in four dogs seven days after occlusion of the external jugular veins. The pressure of the cerebrospinal fluid and the torcular venous pressure are recorded in millimetres of normal saline solution, that in the femoral artery in millimetres of mercury.

animals which were not allowed to survive the anæsthetic had led one to anticipate a normal cerebrospinal fluid pressure, and a venous pressure which was very nearly normal in those which had been allowed to survive twenty-four hours. An attempt was now made to discover some cause for the raised pressures in these animals.

A careful examination was first made of the brain and its coverings in animals in which the external jugular veins had been occluded twenty-four hours previously. The brain and its coverings presented no abnormality either on naked-eye or on microscopic examination, if the precaution were taken to prevent a rapid escape of cerebrospinal fluid before death. There was no evidence of gross dilatation of the superficial vessels of the brain. The intracranial sinuses were free from clot and the external jugular veins were patent close up to the ligatures. The cerebrospinal fluid was normal. On the other hand, the brain usually presented definite abnormalities if the pressure of the cerebrospinal fluid was suddenly reduced before death by allowing quantities of the fluid to escape through the needle in the cisterna magna. The superficial vessels were markedly dilated and a careful scrutiny of the surface with a hand-lens generally revealed minute subpial hæmorrhages. Occasionally these hæmorrhages were abundant, but even then they usually remained discrete and there was never any evidence of gross bleeding. Usually however they were scattered, difficult to find and confined to the base of the brain. When the brains were examined histologically, the hæmorrhages were found to be restricted mainly to the grey matter of the cortex and the basal ganglia. In these cases, the cerebrospinal fluid, although normal to naked-eye inspection, usually gave a slight deposit of blood on centrifuging. There was also a slight increase in the total protein, but this was no more than could be accounted for by the presence of the blood. It is evident that these abnormal findings were directly dependent on the rapid decompression which had preceded death. Somewhat similar observations have been made by Ossipow [7] who found that hyperæmia and hæmorrhages in the brain followed lumbar puncture in dogs.

An attempt was now made to determine whether the return of the intracranial pressures to the region of their original levels within an hour of occluding the external jugular veins was caused by some error in the experimental technique. It was thought at one time that the fall in the pressure of the cerebrospinal fluid could possibly be accounted for by a leakage of cerebrospinal fluid along the side of the recording needle. To minimize the risk of leakage it was the custom always to reject

results obtained from animals in which the dura had been punctured more than once. Nevertheless it was still possible that a gradual leakage of cerebrospinal fluid had occurred along the side of the recording needle. In order to determine whether the fall in pressure could be accounted for on such a basis the following experiments were performed. The external jugular veins were occluded in three dogs. Readings were taken of the venous pressure in the torcular and of the systemic blood-pressure in the femoral artery. At the end of an hour when the venous pressure was noticed to have fallen considerably, the cisterna magna was punctured with a needle and a reading taken of the cerebrospinal fluid pressure. In all three animals the cerebrospinal fluid pressure was found to be within normal limits. The blood-pressure remained steady throughout the experiments.

In the light of these experiments it is inconceivable that the fall in the pressure of the cerebrospinal fluid can be accounted for by a leakage of fluid along the side of the recording needle. The accidental introduction of hypertonic anticoagulant solution into the circulation during the washing out of the cannula employed to record the femoral arterial pressure was also thought to be a possible cause of the fall in the intracranial pressures in the acute experiments. Stringent precautions, however, were taken to avoid the possibility of any of the anticoagulant solution entering the circulation. The anticoagulant employed was an isotonic solution of sodium citrate. It is, therefore, highly improbable that the fall in the pressures could have been brought about in this manner. There does not appear to be any evidence for the belief that the phenomenon is the result of some error in the experimental technique.

It is generally admitted that the rapid rise in the pressure of the cerebrospinal fluid which occurs on occluding the external jugular veins is caused by a reflection of the rise of intracranial venous pressure in that of the cerebrospinal fluid. It would seem important to determine whether the raised cerebrospinal fluid pressure in the animals which had survived twenty-four hours was merely an expression of the raised intracranial venous pressure or whether an increase in the pressure of the cerebrospinal fluid—caused presumably by an increased formation of cerebrospinal fluid—had brought about a state of raised intracranial venous pressure. It is, of course, well known that changes in the pressure of the cerebrospinal fluid are unaccompanied by any change in the venous pressure in the torcular in animals in which the external jugular veins have not been occluded. On the other hand pressure

changes in the intracranial venous system are always reflected in that of the cerebrospinal fluid [1, 3, 8, 9].

Unfortunately no information is available as to whether the pressures react in a similar manner in animals in which the external jugular veins have been occluded. The close similarity between the raised intracranial pressures observed immediately after occlusion of the external jugular veins and the pressures found after a survival period of twenty-

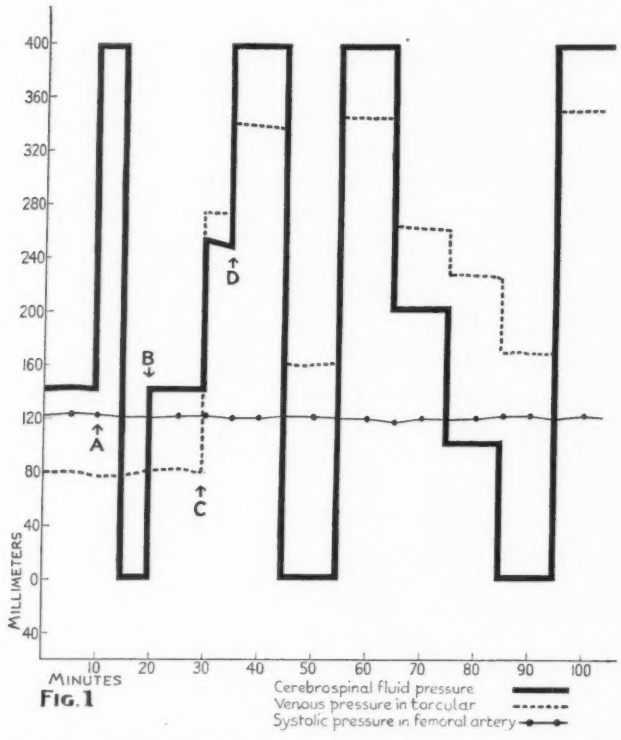

FIG. 1

FIG. 1.—The effect of variations in the pressure of the cerebrospinal fluid upon the venous pressure in the torcular before and after occlusion of the external jugular veins. A reservoir was attached to the manometer recording the pressure of the cerebrospinal fluid at A and the pressure varied. It will be observed that changes in the pressure of the cerebrospinal fluid are without influence on the venous pressure in the torcular. The cerebrospinal fluid pressure was set at its original level at B and at C the reservoir was detached from the manometer and the external jugular veins occluded. After the intracranial pressures had assumed new levels, the reservoir was attached to the manometer at D and the pressure of the cerebrospinal fluid varied. Changes in the pressure of the cerebrospinal fluid are now followed by changes in the same direction but to a lesser extent in the venous pressure in the torcular. The pressure of the cerebrospinal fluid and the torcular venous pressure are recorded in millimetres of normal saline solution, that in the femoral artery in millimetres of mercury.

four hours suggests very strongly that their origin is the same. Experiments were now undertaken to determine the effect of changes in the pressure of the cerebrospinal fluid on the venous pressure in the torcular in animals in which the external jugular veins had been ligated. Changes in the pressure of the cerebrospinal fluid are easily effected by attaching a reservoir containing saline solution to the base of the manometer recording the cerebrospinal fluid pressure. By raising or lowering the reservoir it is possible to set the pressure of the cerebrospinal fluid at any desired level.

Observations were first made on animals shortly after occlusion of the veins and while the intracranial pressures were still high. The investigation was restricted to a study of the effect of changes in positive pressure over a range of 0 to 400 mm. of normal saline solution. A fairly typical experiment is illustrated in fig. 1. The results of the experiments may be briefly summarized. Raising or lowering of the cerebrospinal fluid pressure was accompanied by changes in the same direction in the venous pressure in the torcular. The extent of the change in pressure in the torcular was found to average about 40 per cent. of the change in the cerebrospinal fluid pressure. This was the same both on raising and on lowering the pressures. Occasionally the change in the venous pressure was relatively slight. The smallest change observed in these experiments was 12 per cent. of the change in the pressure of the cerebrospinal fluid; on the other hand it was occasionally as great as 60 per cent.

Observations were also made on animals one hour after the external jugular veins had been occluded and when the cerebrospinal fluid pressure had fallen to the region of its original level. No evidence was obtained which might suggest that the amplitude of the change in the venous pressure was determined by the initial height of the pressures at the start of the experiment. The change in the venous pressure was usually complete after five seconds, and the pressure generally remained stationary after it had attained a new level. In these experiments the pressure of the cerebrospinal fluid was changed at intervals of five or ten minutes.

The experiments were repeated on animals in which the external jugular veins had been occluded twenty-four hours previously. It was found that the torcular venous pressure responded to changes in the pressure of the cerebrospinal fluid in a manner almost identical with that observed in animals immediately after occlusion of the external jugular veins.

Although the above description is that of the most frequent reaction of the venous pressure in the torcular to changes in the pressure of the cerebrospinal fluid after occlusion of the external jugular veins, variations were observed. The following was the most frequent and occurred to some extent in about a quarter of the experiments. A change in the pressure of the cerebrospinal fluid was accompanied by a variation in the same direction in the venous pressure which generally averaged about 40 per cent. of the change in the pressure of the cerebrospinal fluid. When, however, the pressure of the cerebrospinal fluid was restored to its original level, the venous pressure usually returned to a level somewhat higher than its original one. Subsequent manipulations of the cerebrospinal fluid pressure had less and less influence on the venous pressure and a longer period was required for this pressure to attain its new level. Finally, in some experiments the venous pressure remained entirely uninfluenced by changes in that of the cerebrospinal fluid. It was possible to show that clotting of blood in the torcular was not responsible for these results. It would seem highly probable that findings of this type were largely determined by the onset of œdema of the brain and possibly by volume changes in the intracranial vascular system subsequent to sudden lowering of the pressure of the cerebrospinal fluid.

Eyster [4] in 1906 observed during the course of a series of experiments in which it was necessary to maintain the intracranial pressure at a high level for a long period of time, that the brain sometimes became markedly œdematous. He seems to have held the view that the œdema was caused directly by the high intracranial pressure. He states, however, that when the œdema is once established "more or less blocking (of the subarachnoid space) may occur at the isthmus tentorii cerebelli, or at the cranio-vertebral junction."

Masserman and Schaller [5] in 1933 showed that rapid decompression of the ventriculo-subarachnoid space of the dog is followed by œdema of the brain. They believe that this may lead to a "partial œdematous closure of the aqueductus cerebri or subarachnoid block at the foramen magnum." In a more recent paper, Massermann [6] has brought forward evidence that the rapid removal of cerebrospinal fluid in man causes a vascular dilatation in the central nervous system which does not completely regress even if the fluid is immediately reinjected.

We are now in a position to consider whether the results of these experiments justify the conclusion that the raised cerebrospinal fluid pressure found after a survival period of twenty-four hours is directly

dependent on the raised intracranial venous pressure, or whether an increase in the volume of the cerebrospinal fluid has brought about an increase in its own pressure and in the venous pressure in the torcular. Although the experiments provide no evidence against the first of these possibilities, they do, however, show quite clearly that an increase in the pressure of the cerebrospinal fluid in animals in which the external jugular veins have been ligated is accompanied by an increase in the venous pressure in the torcular. It would seem possible, therefore, to account for the pressure findings in the animals which had survived twenty-four hours on a basis of either possibility. The experiments fail to provide us with a means of deciding which explanation is the correct one. It should, of course, be borne in mind that the raised pressures may be due to a combination of causes.

Attention has already been drawn to the fact that the non-recovery experiments were conducted on animals which were fully anæsthetized and in which the anæsthetic was administered at a rate as near constant as possible. A very different state of affairs obtained in the recovery experiments. For a considerable part of the twenty-four hours the animals were active and alert, frequently changing the position of the head in relation to the rest of the body and at times barking or eating their food. It would not be surprising, therefore, if the embarrassed intracranial venous circulation, though able to maintain a fairly normal pressure in the immobile and fully anæsthetized animal, would be unable to do so in the active unanæsthetized animal. It should also be borne in mind that the external jugular veins receive blood not only from the interior of the cranium, but also from the greater part of the muscles and glands of the head. It is well known that during functional activity the blood-flow through these structures is enormously increased. This would add considerably to the embarrassment of the intracranial venous circulation in animals in which the jugular veins have been ligated. It is probable, however, that the most intense degree of venous congestion of the head occurs in these animals as a consequence of the marked embarrassment of respiration during the induction of the ether anæsthesia.

The effect of carbon dioxide on the diameter of the pial arteries of the cat has been carefully studied by Wolff and Lennox [10]. These observers measured the diameter of the pial arteries through a window in the cranium. They found that an increase in the carbon dioxide content of the blood brought about a considerable increase in the size of these vessels. This was usually accompanied by a marked increase

in the pressure of the cerebrospinal fluid. The influence of carbon dioxide on the pial vessels was shown to be independent of changes in the systemic blood-pressure. A marked degree of anoxæmia also had a tendency to increase the size of the vessels, but the effect was comparatively slight compared with that of carbon dioxide. Normally an increase in the oxygen content of the blood resulted in a very slight decrease in the diameter of the arteries. The influence of carbon dioxide, however, almost completely obscured that of oxygen. These workers also made the important observation that a dilatation of the vessels was more readily produced than a constriction. When the

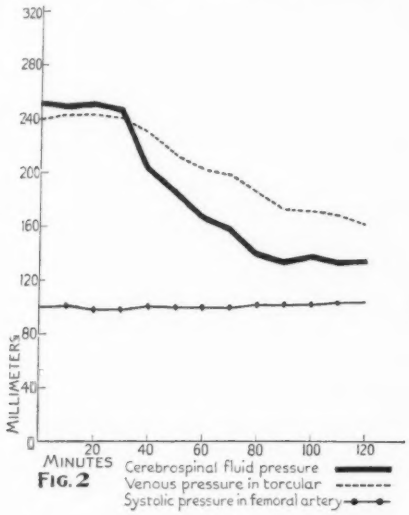

FIG. 2

FIG. 2.—The effect of continuous anæsthesia on the intracranial pressures of an animal in which the external jugular veins have been occluded for twenty-four hours. The pressure of the cerebrospinal fluid and the torcular venous pressure are recorded in millimetres of normal saline solution, that in the femoral artery in millimetres of mercury.

composition of the respired gas was altered, respiration was affected before either the systemic arterial blood-pressure or the size of the pial arteries.

It must be admitted that this explanation of the high intracranial pressures in the survival experiments is mainly speculative. If, however, it is correct, the intracranial pressures should be found to fall considerably after complete anæsthesia has been achieved and the administration of the ether is maintained at a constant rate. The cerebrospinal fluid pressure, the torcular venous pressure and the arterial

pressure in the femoral artery were now recorded in a number of dogs in which the external jugular veins had been occluded twenty-four hours earlier. The anæsthesia was maintained and the experiments were continued for several hours. By the end of the first hour the cerebrospinal fluid pressure had usually attained normal levels. A fall also occurred in the venous pressure in the torcular, but it was not so rapid or so complete, and at the end of the second hour it was higher than that of the cerebrospinal fluid. Throughout the experiments the arterial pressure in the femoral artery remained steady. A typical experiment is illustrated in fig. 2. The pressure changes in these experiments are identical with those observed in the acute experiments, except for a slightly longer period required for the pressure of the cerebrospinal fluid to return to normal levels. Now it is known that the raised pressure of the cerebrospinal fluid in the acute experiments is directly dependent on the raised intracranial venous pressure. It would seem reasonable, therefore, to conclude that the raised pressure of the cerebrospinal fluid in the recovery experiments has a similar origin.

The maximum duration of the acute experiments was three hours; at the end of this period the pressure of the cerebrospinal fluid was at a normal level, and although the venous pressure in the torcular was considerably reduced it was still somewhat higher than its original level. It has been suggested that the raised intracranial pressures in the experiments with a twenty-four hours recovery period were due either to an extra strain imposed on the intracranial venous circulation during the active recovery period, or to the cerebral congestion which occurs during the initial stages of the ether anæsthesia. If the latter view be correct it might be expected that the intracranial pressures would be found to be high even after a recovery period as short as one or two hours. In order to test this possibility the external jugular veins were occluded in two dogs. The animals were then allowed to recover from the anæsthetic and an hour and a half later they were again anæsthetized and a record taken of the intracranial pressures. It will be observed from Table IV that the pressures were of the same order as those found in the experiments with a more prolonged recovery period. The cerebrospinal fluid pressure and the torcular venous pressure also resemble in their relative heights the pressures found immediately after occlusion of the external jugular veins. This may perhaps indicate that the pressures have only just been raised. On maintaining the anæsthesia the cerebrospinal fluid pressure was found to have returned to normal levels after about an hour, although at that

time the venous pressure was still higher than the normal. Although these experiments suggest very strongly that the raised intracranial pressures in the experiments with a recovery period were caused by the venous congestion which occurred during the initial stages of the ether anæsthesia, it must nevertheless be admitted that the experiments do not exclude the possibility that the pressures may be higher than normal during the period of recovery. No method is yet available by which the intracranial pressures can be recorded in the conscious animal.

TABLE IV.

Dog No.	Cerebrospinal fluid	Torcular venous	Femoral artery
1	(*a*) 220	230	115
	(*b*) 130	145	120
2	(*a*) 210	205	95
	(*b*) 135	170	95

The cerebrospinal fluid pressure, the torcular venous pressure and the arterial pressure in the femoral artery in two dogs in which the external jugular veins have been occluded. The animals were allowed to recover from the anæsthetic as soon as the vessels had been occluded and one and a half hours later they were again anæsthetized and a continuous record taken of the intracranial pressures.

(*a*) The pressure levels after complete anæsthesia had been attained.

(*b*) The pressure levels after anæsthesia had been maintained for one hour. The pressure of the cerebrospinal fluid and the torcular venous pressure are recorded in millimetres of normal saline solution, that in the femoral artery in millimetres of mercury.

It is noteworthy that it has been unnecessary to postulate an increased formation of cerebrospinal fluid in order to account for any of the phenomena associated with a prolonged occlusion of the external jugular veins.

Summary.

(1) The intracranial pressures were found to be raised in animals in which the external jugular veins had been ligated for twenty-four hours. A careful examination after death of the brains and their coverings failed to reveal any cause for the high pressures.

(2) A study was made of the effect of changes in the pressure of the cerebrospinal fluid on the venous pressure in the torcular in animals in which the external jugular veins had been occluded. Changes in the pressure of the cerebrospinal fluid were found to be accompanied by changes in the same direction, although to a lesser degree, in the venous pressure at the torcular.

(3) An increased formation of cerebrospinal fluid was not, however, considered to be the cause of the raised pressures in the animals in

which the external jugular veins had been occluded for twenty-four hours. Experiments are described which suggest very strongly that the raised pressure of the cerebrospinal fluid was directly dependent on the raised intracranial venous pressure. It was also considered probable that the intracranial venous pressure had been raised during the initial stages of the ether anæsthesia.

REFERENCES.

[1] Becht, F. C. *Amer. Journ. Phys.*, 1920, **51**, 1.
[2] Bedford, T. H. B. *Brain*, 1934, **57**, 1.
[3] *Idem. Ibid.*, 1935, **58**, 427.
[4] Eyster, J. A. E. *Journ. Exper. Med.*, 1906, **8**, 565.
[5] Masserman, J. H., and Schaller, W. F. *Arch. Neur. and Psych.*, 1933, **30**, 107.
[6] Masserman, J. H. *Ibid.*, 1934, **32**, 523.
[7] Ossipow, V. P. *Deutsch. Ztschr. Nervenh.*, 1901, **19**, 350.
[8] Weed, L. H., and Hughson, W. *Amer. Journ. Phys.*, 1921-22, **58**, 101.
[9] Weed, L. H., and Flexner, L. B. *Ibid.*, 1933, **105**, 266.
[10] Wolff, H. G., and Lennox, W. G. *Arch. Neurol. and Psych.*, 1930, **23**, 1097.

PRIMARY TUMOURS OF THE ROOT OF THE FIFTH CRANIAL NERVE: THEIR DISTINCTION FROM TUMOURS OF THE GASSERIAN GANGLION.[1]

BY HUGO KRAYENBÜHL (ZURICH).

TUMOURS of the 5th nerve and its ganglion were formerly so rarely recognized that they were regarded as pathological curiosities, and their symptomatology was poorly defined. With the development of interest in neurosurgery during the last two decades, an increasing number of these tumours has been reported in the literature, and the possibility of successful radical treatment has become apparent. Hitherto case reports have been concerned for the most part with primary and secondary tumours of the Gasserian ganglion, and little is known of the tumours that arise in the retro-ganglionic root of the nerve.

In this paper it is proposed to report two cases of tumour arising from the nerve root, and to show by an analysis of the primary tumours reported in the literature that there is considerable difference between the clinical picture of tumours of the ganglion and that of tumours of the nerve behind the ganglion. The clinical distinction is important because the method of operative approach should differ radically in the two groups of cases. Few attempts have been made as yet to remove retro-ganglionic tumours, doubtless because the clinical picture produced by the tumour is insufficiently known.

Case 1.—*Neurofibroma of left 5th nerve. Three years' history of cerebello-pontine angle disturbances. Lumbar puncture. Rapid exitus.*

History.—J. D., a lorry driver, aged 55, was admitted to the London Hospital under the care of Dr. Russell Brain on April 6, 1935. He had enjoyed good health until three years before admission, when he began to have in the mornings shooting pains in the left side of the head. These started in the left temple and spread to the occiput. As time went on the pain became more severe and continuous, and he lost his employment. One year before admission he began to stagger to the right and to suffer from attacks of giddiness, which increased in severity and frequency. For two to three months he had noticed that the sight of the left eye was failing, that his teeth and gums on the left side felt numb, and this was followed by weakness of the left side of the face with difficulty in mastication, swallowing and speaking. He

[1] From the Department of Neurosurgery, the London Hospital.

complained also that all foods tasted alike. He had become deaf in the left ear and had a feeling of numbness and weakness of the right hand, and his memory had become poor.

Examination.—The positive signs were as follows: Bilateral anosmia. Bilateral papillœdema with severe impairment of vision. Lateral and upward nystagmus. Absence of both corneal reflexes. Anæsthesia and analgesia of the left side of the face, complete over the ophthalmic division and partial over the maxillary and mandibular divisions. Normal power in masticatory muscles. Severe upper and lower facial weakness on left side with constant dribbling of saliva from the left corner of the mouth. Deafness in the left ear. Hypotonia of all limbs and slight weakness of the right upper limb. Absence of all abdominal reflexes. Extensor plantar response on the left side.

X-rays showed no signs of increased intracranial pressure, but the dorsum sellæ and posterior clinoid processes were eroded. The cerebrospinal fluid showed no excess of white cells; the total protein was raised to 110 mgm. per cent. A few hours after lumbar puncture the patient became comatose: his temperature rose to 109° F., and he died. A clinical diagnosis of left acoustic neurinoma had been made.

Necropsy.—(P.M. 152, 1935). Examination was limited to the head. In the brain there was slight flattening and broadening of all convolutions of the anterior three-quarters of the convexities: slight downward projection of the gyrus rectus on each side; very slight foraminal herniation of the left cerebellar tonsil, which was displaced slightly to the right and forwards against the medulla. There was considerable whitish opacity of the leptomeninges over the cerebral convexities.

In the left cerebello-pontine angle was a smooth, firm, lobulated, greyish-white translucent tumour, 4·2 by 2·6 cm., compressing the left side of the pons and projecting backwards into the left cerebellar lobe (fig. 1). Medially it was in contact with the basilar artery throughout the greater part of its course. Caudally it extended down to the left 9th, 10th and 11th nerves, and laterally it was in contact with the petrous bone, but not attached to it, and the porus acusticus was normal. Rostrally it extended forwards through the dural opening into the cave of Meckel, where it formed a mass (2·2 by 1·8 by 1·2 cm.) in the position of the Gasserian ganglion (fig. 1 E), which indented the underlying bone.

The left 5th nerve was only found after the tumour had been tilted from its bed (fig. 1 B, C, D). In the proximal 1 cm. of its course it lay on the medial and dorsal aspect of the tumour, flattened betweeen the pons and the tumour. Then passing distally it divided into two flattened semi-transparent bands, 0·1 by 0·2 cm. wide, which entered the capsule of the tumour and then spread out into numerous ill-defined bundles. These bundles, in places difficult to distinguish from thicker parts of the capsule, ran for varying lengths on the dorsal surface of the tumour and then disappeared into its substance. At the level of the caudal end of the cave of Meckel no nerve-fibres could be seen on the surface of the tumour. In the

cave of Meckel no trace of normal Gasserian ganglion could be detected, but only tumour (fig. 1 E). At the rostral end of the tumour all three divisions of the trigeminal nerve could be found, the third and second divisions possessing a normal appearance while the first division was small and flattened.

The left 4th nerve lay immediately cephalic to the apex of the growth. The left 6th nerve ran from its origin transversely across the ventral aspect

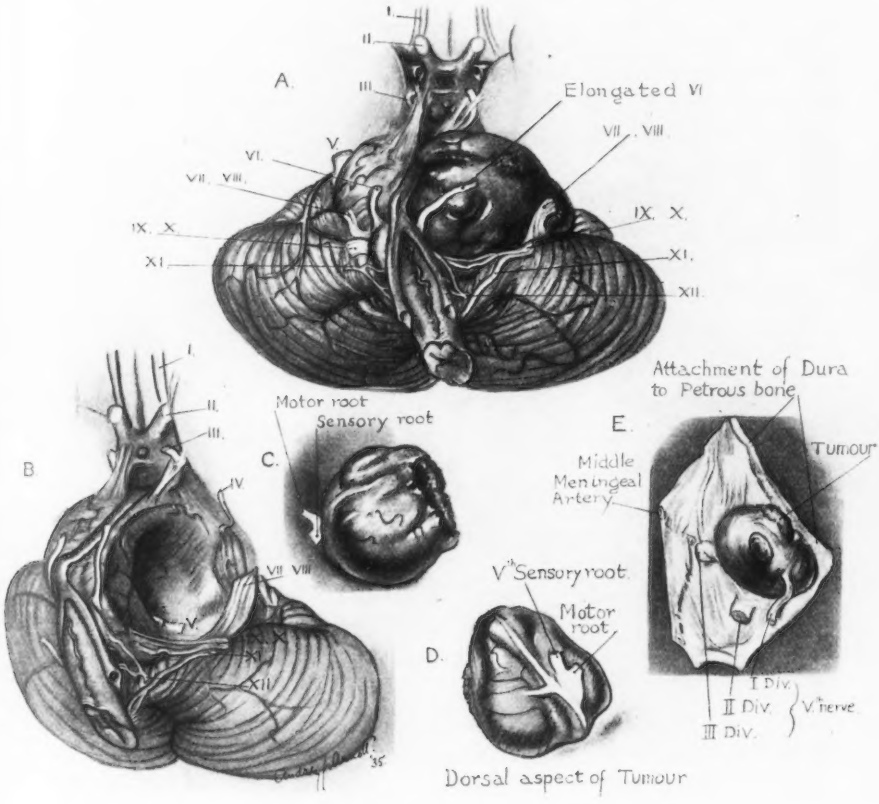

FIG. 1.—*Case* 1. Neurofibroma of the left 5th cranial nerve.

of the tumour. The left 7th and 8th nerves emerged between the ventral surface of the cerebellum and the adjacent ventral and outer surface of the tumour (fig. 1 A).

Sections through the tumour showed it to be composed of numerous cysts up to 1·3 cm. in diameter, and soft, glistening, translucent, grey tissue. The

centre was occupied by large areas (about 2·3 cm. in diameter) of recent hæmorrhage, the greater part of which lay within cystic spaces. The part of the tumour adjacent to the pons was of a somewhat firmer consistency than the rest. In the cave of Meckel the tumour was firm, and pearly grey with numerous central cystic spaces up to 0·6 by 0·4 cm., and showed to the naked eye no traces of nerve-fibres or ganglion.

Microscopic examination.—Two sections were taken from the tumour in the posterior fossa, one of its rostral portion and the adjacent border of the pons, and the other of a portion with the flattened 5th nerve root attached to it. Two coronal sections were also taken of the tumour in the region of the left Gasserian ganglion, one through its greatest thickness and the other through its rostral end to include the three divisions of the trigeminal nerve.

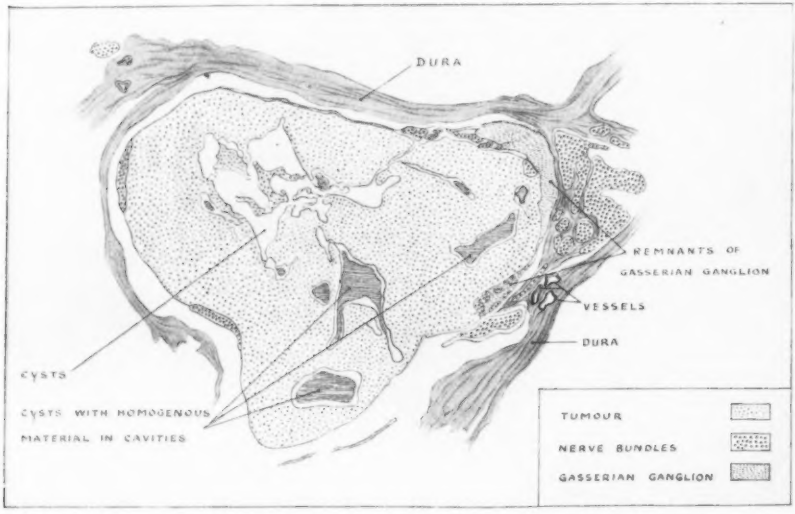

FIG. 3.—*Case* 1. Schematized projection drawing of coronal section of Gasserian ganglion showing relationships of tumour. (Insert conventions adopted).

The tumour mass in the posterior fossa is composed of closely packed spindle-shaped cells with indefinite margins. These cells mostly lie parallel to one another in sheaves, forming interlacing bundles. Their nuclei are oval or even rod-shaped; they have a wide-meshed net of delicate chromatin and usually a single small nucleolus. Mitotic figures are not seen. The cytoplasm has a delicate fibrillar structure. With Mallory's phosphotungstic acid hæmatoxylin the fibrils can occasionally be demonstrated. With Laidlaw's silver carbonate method for reticulum fibres many areas contain abundant very delicate parallel fibres which form interlacing bundles (Plate IV, fig. 2). Collagen fibres, as demonstrated with van Gieson's stain, are restricted to the walls of blood-vessels and their immediate neighbourhood. The tumour cells

PLATE IV.

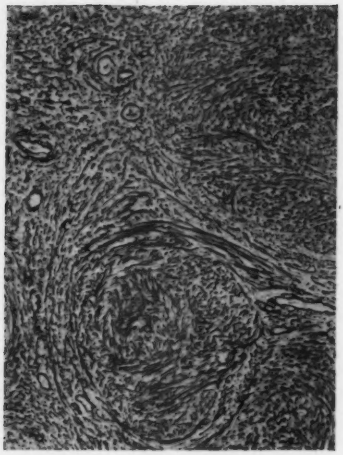

FIG. 2.

FIG. 4.

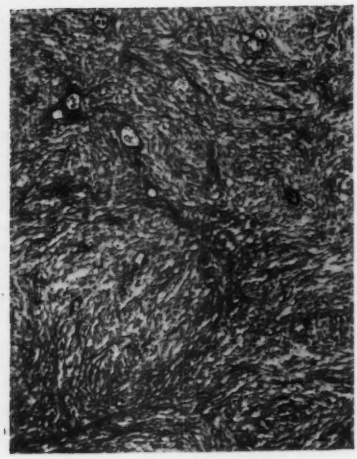

FIG. 6.

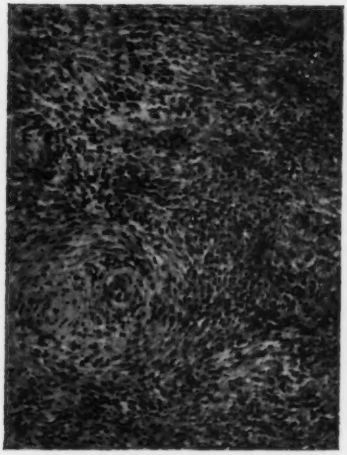

FIG. 7.

FIG. 2.—*Case* 1. Tumour in Gasserian ganglion showing reticulin fibrils. Laidlaw. × 100.

FIG. 4.—*Case* 1. Tumour in Gasserian ganglion, a portion of which is seen below. Hæmatoxylin and eosin. × 98.

FIG. 6.—*Case* 2. Tumour showing reticulin fibrils. Laidlaw. × 100.

FIG. 7.—*Case* 2. Tumour showing whorled arrangement of cells. Hæmatoxylin and eosin. × 118.

To illustrate paper by Hugo Krayenbühl.

sometimes form concentric nests about the blood-vessels or lie in whorls independent of a vascular core. The arrangement of the nuclei is occasionally suggestive of palisading, but this is nowhere pronounced.

In the deeper parts of the tumour the arrangement of the cells is frequently much less definite; the fibrillar structure of the cytoplasm is absent and the spaces between the nuclei are occupied by fine anastomosing strands of cytoplasm. These areas merge into others where degeneration is clearly indicated by the loss of nuclei, and every transition can be demonstrated between this and cyst formation. In the walls of the cysts and elsewhere are occasional collections of macrophages containing iron pigment.

This part of the tumour, lying in the posterior fossa, is enclosed by a thin collagenous capsule derived from the leptomeninges. Nerve fibres are not seen inside the tumour, they are only present in the capsule.

Both sections through the Gasserian ganglion region show a central mass of tumour tissue continued forwards from the main tumour in the posterior fossa (fig. 3). It presents histological features similar to those that have already been described, except that fibrils were not demonstrated with phosphotungstic acid hæmatoxylin. Investing the tumour tissue is a layer of delicate interlacing collagenous fibres of variable thickness, the outer surface of which is coated with a single layer of greatly flattened cells. In this layer are incorporated the Gasserian ganglion and bundles of nerve-fibres. The Gasserian ganglion forms a thin crescentic mass on the dorsal aspect, and its cells are of normal appearance and shape, except for a few degenerative changes (Plate IV, fig. 4). The nerve-fibres, which are myelinated, are distributed all over the capsule of this part of the tumour either as well-defined bundles surrounded by an endothelial capsule, or as isolated fibres. A few individual fibres pass into the adjacent tumour, but they are confined to its superficial parts. The tumour does not invade the dura of the cave of Meckel, but is separated from it by a thin space lined by a single layer of greatly flattened cells which obviously represents the subdural space.

Comment.—The anatomical and histological features of this tumour leave little doubt that it is a neurofibroma of the trigeminal nerve. Histologically it resembles the corresponding tumours that arise on the 8th nerve, both in the morphology of its cells, the abundant though focal production of reticulum fibres, and in its tendency to undergo cystic degeneration. The main bulk of the tumour was situated in the cerebellopontine angle, the 7th and 8th nerves formed a large bundle that was not connected with the tumour, and the fibres of the 5th nerve were in their proximal part spread out in the capsule and in their distal part lost in the substance of the tumour. The tumour was invested by the leptomeninges and not attached to the dura.

The rostral portion of the tumour occupied the cave of Meckel, but there was no evidence that the tumour arose in the Gasserian ganglion,

since histological examination showed flattened but otherwise normal components of the ganglion spread out over the dorsal surface of the tumour. An identical relationship of the ganglion to a tumour of the trigeminal nerve has been demonstrated in a recent example of v. Recklinghausen's central neurofibromatosis (P.M. 316, 1935), in which diffuse tumours were present on both trigeminal nerves as well as upon many other cranial and spinal nerve roots. It may be presumed, therefore, that the tumour in Case 1 arose in the sheath of the trigeminal nerve behind the ganglion.

This case had not been completely investigated, especially as regards hearing and vestibular functions, at the time when the unfortunate catastrophe occurred following lumbar puncture. However, even with full investigations it is doubtful whether the provisional diagnosis of acoustic neurinoma would have changed, for most of the clinical features of the case fitted closely the clinical picture of acoustic neurinoma. Although the illness was of three years' duration numbness in the trigeminal area was only complained of three months before death. And pain in the face was entirely absent; this is characteristic of most tumours of the trigeminal root.

Most of the cases reported in the literature could not be distinguished with certainty from acoustic neurinoma, but the following case is representative of a small group in which differential diagnosis is possible by virtue of severe primary trigeminal symptoms and other features.

Case 2.—*Neurofibroma of right trigeminal nerve. Six years' illness of headache, sensory disturbance in right side of face, staggering, deafness, mental deterioration, &c. Death.*

History.—W. P., a male dust destructor worker, aged 55, referred by Dr. Flood, was first admitted to the London Hospital on June 27, 1931, on account of headaches and attacks of unconsciousness. From the age of 2, he had had a squint of the right eye, attributed to a fall on the head. In July, 1926, his right testicle had been removed for swelling, associated with hæmaturia.

In January, 1927, he began to suffer from short attacks of headache, for the most part in the right temporal region, but sometimes extending to the neck and then accompanied by stiffness. This headache was not frequent at first, and he continued at work. But gradually it became more intense, and the attacks, which lasted from half to one minute, occurred a dozen times a day. From the onset of the illness he had also had at times a feeling of numbness on the right side of the forehead and right side of the face, as though it were stiff and starched. In the same part of the face he had at times

some pain, but had never considered this symptom as a major part of his complaint.

In 1929 his vision began to fail. He staggered to the left when walking, began to drop things held in the left hand and his left foot was sometimes observed to twitch during the night.

In November, 1929, he was admitted to Charing Cross Hospital under the care of Dr. Gordon Holmes, to whom we are indebted for the following information: The right eye was almost immobile, drawn outward and slightly down; the visual fields were diminished from the periphery. Analgesia was found on the right side of the face, and weakness of the right masseter muscle. Deafness was bilateral, more marked on the right than on the left. There was a diminution of power and co-ordination in the left upper and lower limbs and the outstretched left upper limb was not well maintained. The left knee-jerk was brisker than the right and the left plantar response was extensor. Protein in the cerebrospinal fluid was slightly raised, being 0·050 per cent., with a very faint excess of globulin, and one white cell per c.mm. Dr. Holmes made a diagnosis of a very slowly progressing cerebral tumour involving the right 5th nerve and considered that an operation was inadvisable.

The patient returned to work, but had to give it up a few weeks later because of disturbance of gait. He was walking like an intoxicated man and dragging the left foot. Though at times his balance seemed to improve slightly, he could not walk without support. When bending forwards he often experienced a feeling of giddiness, but external objects did not appear to rotate. Trembling of both hands, worse on the left side than on the right, also developed at this stage.

In September, 1930, the patient had an attack of stupor which lasted nearly two months; he did not seem to know anybody or to realize that he was in bed or what was being done for him; he would answer if spoken to, but never spoke voluntarily; he was incontinent of urine and fæces. He gradually recovered from this attack, but from that time his memory failed progressively, his intelligence deteriorated, and his emotional reactions gradually became excessive. At this stage he also began to notice that he could not masticate on the right side. He thought, too, that there was a loss of sensation in his mouth. Tinnitus was present at times, but never severe.

Examination. June, 1931.—The patient was a man of low intelligence and deficient memory. Smell was diminished at both nostrils; both optic discs were flat; there was an external squint and amblyopia of the right eye; upward movement of the left eye was diminished. Visual acuity: $\frac{2}{24}$ on the right, $\frac{6}{18}$ on the left side. The right corneal reflex was absent; there was very slight relative anæsthesia to cotton-wool on the right side of the face, relative analgesia in the right ophthalmic division and slight deviation of the jaw to the right.

Other symptoms were slight left lower facial weakness; bilateral incomplete deafness, more marked on the right than on the left; slight flaccid paresis of the left upper and lower limbs; increased tendon-jerks and an extensor plantar

response on the left side; gait slow, on a wide base, with a tendency to fall to the right; normal sensibility to posture, cotton wool and pin-prick.

X-rays showed a fairly thin vault without increase of convolutional markings. The sella turcica was of normal size, but the posterior clinoid processes appeared to be eroded. Ventriculography showed bilateral symmetrical hydrocephalus of moderate degree. No surgical treatment was undertaken, because, from the evidence of pressure upon the right cerebral peduncle, it was considered that the lesion was inaccessible.

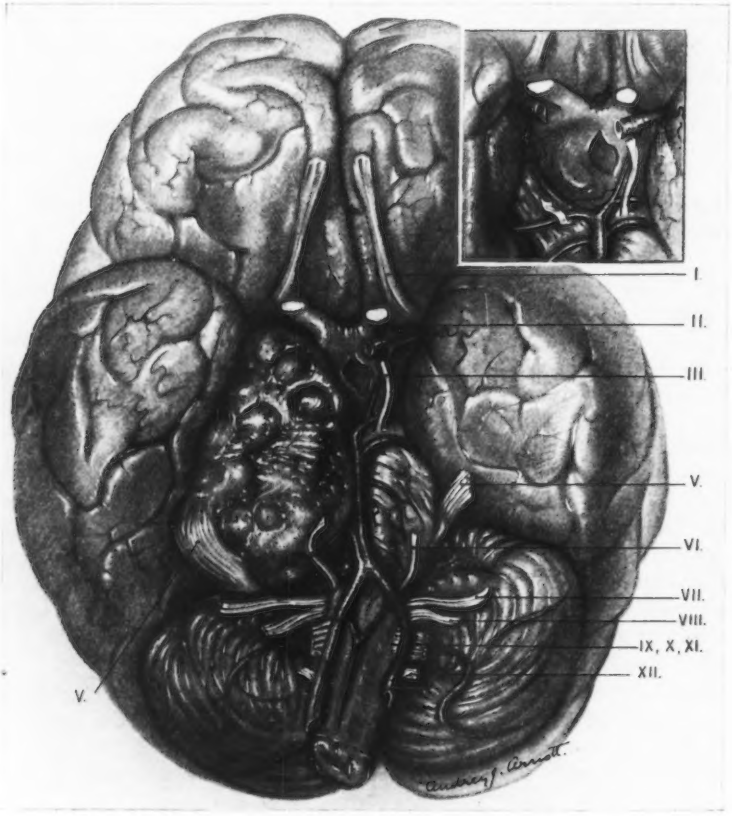

FIG. 5.—*Case* 2. Neurofibroma of the right 5th cranial nerve.

Subsequent course.—After his discharge on July 11, 1931, the patient grew gradually worse, and was in bed at home most of the time. He was readmitted to hospital in February, 1933. His mental condition had further deteriorated; he was incontinent of urine, partially disorientated and very drowsy. There

was still no papillœdema, the right corneal reflex was greatly diminished and there was analgesia over the right forehead and over the right side of the nose, but the sensibility on the lower part of the face was still within normal limits. All limbs were spastic and there was now a bilateral extensor response. The patient went home again, and a few weeks later lapsed into coma and died.

Necropsy. (P.M. 605, 1930, Appendix).—The brain was obtained through the kindness of Dr. Deacon. When it was removed from the skull a large, greyish white, smooth, encapsulated, soft tumour was disclosed situated in the posterior fossa, extending through the tentorium into the middle fossa, where it appeared to replace the right trigeminal nerve and the Gasserian ganglion. Unfortunately the middle fossa extension of the tumour was not removed completely, but a small portion of it was taken for section.

Examination of the brain after fixation.—A tumour measuring 7·0 by 4·0 by 2·5 cm. lay in the right cerebellopontine angle and extended forwards into the cave of Meckel and beneath the floor of the third ventricle (fig. 5). It was embedded in the ventral surface of the right side of the floor of the third ventricle. Anteriorly and laterally the dorsal surface of the tumour indented the ventral surface of the hippocampal gyrus which was flattened between the tumour and the right cerebral peduncle. Caudally and laterally the growth lay in contact with the right middle cerebellar peduncle and excavated slightly the anterior end of the right anterior crescentic lobule.

The right 7th to 12th cranial nerves lay on the caudal side of the tumour and were not in contact with it, at any rate, not in the proximal part of their course. The right 7th nerve was flattened to a translucent grey strand less than 0·05 cm. wide which passed over the ventral surface of the tumour.

At its junction with the pons the right 5th nerve was separated into two parts by the tumour; the greater part of it passed over the ventrolateral aspect of the tumour as a broad splayed-out strand of fibres 0·7 cm. wide, which is shown in fig. 5; the smaller and less flattened part crossed the dorsolateral aspect of the tumour. At its origin the nerve was distinct from the tumour, but in its more distal part it was spread out diffusely and incorporated in the capsule of the tumour.

The right 3rd and 4th nerves lay on the dorsal aspect of the tumour. From its origin the right 3rd nerve passed in a caudal direction to loop around the posterior cerebral artery, being thinned at that point (fig. 5). It then came forward over the dorsal-cephalic surface of the tumour, fairly closely attached to its capsule over a length of 2·5 cm. In this part of its course it was flattened almost to translucency and to a width of 0·6 cm. by tumour nodules that projected into it. The posterior half of the right optic tract was flattened and displaced outwards by the tumour immediately below it. The tumour did not reach the optic chiasm.

Coronal sections through the brain showed a moderate degree of symmetrical dilatation of the lateral ventricles and a considerable dilatation of the third ventricle.

The tumour was sharply circumscribed by a smooth, and in places,

glistening white and greyish-white and yellowish-white translucent tissue in which were several empty cysts up to 2·5 cm. in diameter. These cysts were lined for the most part with smooth glistening tissue and crossed by white septa or fine trabeculæ.

Microscopic examination.—Sections were taken through the tumour of the posterior fossa and the adjacent pons and through fragments of the tumour of the middle fossa.

The tumour in the posterior fossa is closely apposed to the pons and the leptomeninges here form the capsule of the tumour. They are infiltrated with lymphocytes and macrophages, many of which contain iron pigment. There is no invasion of the pons by tumour. Histologically the tumour itself is identical in appearance with the one described in the preceding case (Plate IV, figs. 6 and 7), except in the following particulars. The amount of cystic degeneration in the interior of the tumour is greater, the cysts being both larger and more numerous. There is a correspondingly greater amount of degeneration in the adjoining tumour tissue and throughout large areas the cell nuclei have disappeared or have been replaced by collections of macrophages containing iron pigment. Small bundles of myelinated nerve fibres are present in different parts of the tumour, usually near the periphery. In two places these fibres run straight through the tumour and are accompanied by a few psammoma bodies.

The fragments taken from the middle fossa include a few collections of ganglion cells. These are surrounded by their capsular cells and appear normal. They are evidently derived from the Gasserian ganglion, but their precise relationship cannot be stated.

Comment.—This tumour resembled closely in its macroscopic and microscopic appearances the tumour in Case 1 and may, therefore, be classed as a neurofibroma. It is unfortunate that the middle fossa extension of the tumour was not removed completely at the necropsy, and that the precise relation of the tumour to the Gasserian ganglion is therefore not known. However, in the fragments from the middle fossa that were available ganglion and capsular cells were of normal appearance and it is reasonable to assume, therefore, that the tumour did not arise in the Gasserian ganglion. As in Case 1 the tumour probably took its origin from the distal part of the root. Whether it arose from the root behind or within the cave of Meckel it is impossible to say. In this connection, however, it may be noted that in the two cases of small "Schwannoma" reported in the literature (Alajouanine, de Martel, Oberling and Guillaume [1] and Alajouanine, Thurel and Guillaume [2]) the tumour lay on the nerve just behind the level of the apex of the petrous bone.

In the clinical course of our two cases the most striking feature is

the inconspicuous character of the subjective trigeminal symptoms, and especially the complete or almost complete absence of pain. In Case 1 a feeling of numbness in the second and third divisional areas of the affected nerve came on only in the last three months of the illness. In Case 2 a feeling of numbness over all three divisional areas was present at times during the whole illness, but was overshadowed by other symptoms; pain in the face was felt at times but was never severe. On examination anæsthesia and analgesia were present in both cases and in one case the motor root was also slightly affected.

Analysis of the reported cases shows that absence of pain in primary tumours of the trigeminal root is by means unusual, and that this fact is in marked contradistinction to what happens in primary tumours of the Gasserian ganglion. I have been able to find in the literature 54 cases of primary tumour of the Gasserian ganglion or trigeminal root. From the pathological reports it is only possible in 29 cases to be certain as to the exact origin of the tumour, whether from the ganglion or from the root. In 26 cases the tumour arose from the ganglion. In 2 of them the clinical reports were incomplete [15, 42], but in every one of the remaining 24 severe continuous pain of the face of an aching, throbbing or burning character was the initial symptom and persisted throughout the whole illness. In the 3 cases in which the tumour clearly arose from the trigeminal root, pain in the face was absent during the whole course of the illness in two (Glaser [7], Alajouanine, Thurel and Guillaume [2]), and was of only moderate degree in the third (Alajouanine, de Martel, Oberling and Guillaume [1]).

If the 54 cases from the literature are studied from the clinical standpoint it is possible from the order in which symptoms appeared to form an opinion in every case as to the probable origin of the tumour in the middle or posterior fossa. In 39 cases with an onset pointing to the middle fossa all had severe facial pain. In 13 of these cases the tumour extended into the posterior fossa, and pain remained constant except in the cases of Dew [20] and Nowotny and Uiberall [34], where it disappeared after six months and two years respectively. The 15 cases with an onset pointing to the posterior fossa (as indicated by lower cranial nerve palsies, cerebellar or cerebral peduncle signs) had marked pain in 2 cases, slight pain in 5 cases and none in 8 cases.

The outstanding fact is that in 56 cases of tumour of the Gasserian ganglion and the trigeminal root, if the two cases of this paper are included, there were 15 cases in which facial pain was slight or absent. From this analysis of the literature it is probable that pain occurs when

the ganglion is primarily involved and is usually absent when the tumour begins on the trigeminal root. It is not surprising that when primary root tumours spread to the ganglion pain does not occur; for by that time conduction of impulses centrally is impaired by destruction of fibres in the root. This explanation is in accord with the view of Pierre Marie when he reported his case of root tumour [11].

These trigeminal root tumours provide a variety of initial symptoms. A closer study of the 2 cases reported in this paper and the 15 cases from the literature reveals a definite symptomatology of cerebello-pontine angle involvement, 2 cases presenting vertigo, 2 tinnitus, 3 tinnitus and deafness, 2 unsteadiness in walking associated with vertigo, and 1 facial spasm. In our own 2 cases unilateral headache and in another case failure of vision was the first symptom. Only 2 cases were initiated by a sudden facial numbness, and in 1 case a feeling of coldness in the face associated with toothache on the same side was the first symptom. The case reported by Alajouanine, de Martel, Oberling and Guillaume is the only one in this series in which facial pain was present from the very beginning.

During the further course of the illness trigeminal symptoms became more conspicuous, but they are by no means so severe as one might have expected. In 14 cases subjective trigeminal symptoms were present: the feeling of numbness, coldness and tingling was a prominent symptom from periods varying from several weeks to several months in 10 cases, and was in 5 instances at times associated with slight facial pain. Four cases presented at times some pain, but it was severe and constant in only two instances (Shelden [14], Alajouanine, de Martel, Oberling and Guillaume [1]). In 3 cases, each of them thoroughly studied, no subjective trigeminal symptoms were recorded at all (3*a*, 3*b*, 9).

The objective evidence of trigeminal affection gives a picture very different from that suggested by the subjective symptoms, as sensory loss was marked in the whole series. In one case (Petrina and Klebs [13]) the physical examination is incomplete. Of the remaining 16 cases, 10 had either complete or relative anæsthesia and analgesia over one entire side of the face, 2 were affected in the first and 2 in the second divisional area alone, and in 1 case the first and second, and in another the second and third branch were involved. The corneal reflex was diminished or absent on the side of the tumour in 10 cases and was impaired on both sides in 2 cases. Ulceration of the cornea is reported twice, and the motor branch showed weakness and partial atrophy of the masticatory muscles in 7 cases.

Deafness is as a rule one of the earliest symptoms in the course of these tumours, and it has been reported three times as an initial symptom. Generally its onset is gradual, but it steadily increases until it is almost complete. It is reported in 13 out of the 17 cases, and twice, as in Case 2, it was bilateral, but much more marked on the side of the tumour. Caloric tests were done in 5 cases and showed an impairment of the vestibular function on the side of the tumour. Tinnitus has been recorded only five times, and was then present from the very beginning. Facial weakness was noticed in half the cases, and involvement of the 9th, 10th, 11th, and 12th cranial nerves was reported in 11 cases. Staggering gait was present ten times, and was often associated with vertigo and homolateral ataxia.

Evidence of involvement of the cerebral peduncles is of special interest in the diagnosis of these tumours, as shown in our Case 2. In 4 cases contralateral pyramidal signs were reported, and in 3 cases they occurred on the homolateral side.

Intracranial pressure is, as a rule, only moderately raised in these tumours. Headache was present in 9 cases and was usually not severe. It reached an intense degree only in our 2 cases, where it was strictly unilateral. Moderate papillœdema and some optic atrophy was noticed in 25 per cent. of the cases, and failure of vision occurred five times. Vomiting was reported only twice. From these facts it is probable that the rate of growth of these tumours is slower than that of acoustic tumours.

The analysis of the symptoms of the reported cases shows that the diagnosis of a trigeminal root tumour is by no means easy. The main difficulty is to distinguish between a tumour of the trigeminal root and a tumour of the acoustic nerve. In acoustic tumours the degree of deafness and vestibular loss is usually greater than the degree of trigeminal sensory loss on the side of the lesion, but not invariably so. In trigeminal root tumours, however, the degree of objective trigeminal sensory loss is not always greater than the degree of deafness, so far as can be judged from the information at present available. Consequently there are many cases in which a precise differential diagnosis could not be made. However, in certain cases forward extension of a trigeminal root tumour at a relatively early stage of the illness will give distinctive signs. Thus, in our Case 2 the early sensory and motor involvement of the trigeminal nerve, coupled with evidence of pressure on the adjacent cerebral peduncle, gave a clinical picture from which the correct diagnosis was made. A further aid to diagnosis of trigeminal root

tumours is derived from the fact that these tumours, in their almost invariable extension forwards into the middle fossa, often produce ocular palsies. These occurred seven times in the 17 reported cases, and were described as 3rd, 4th and 6th nerve palsies. In two instances also a Horner-Claude Bernard syndrome was noticed as a result of pressure by the tumour on the sympathetic fibres of the internal carotid plexus.

Help may sometimes be obtained from radiographic examination of the skull. In most of the cases the reported radiological investigations were negative, but in the case reported by Nowotny and Uiberall [12] X-rays showed erosion of the apex of the petrous bone and of the floor of the middle fossa in the region of the cave of Meckel. Similar appearances in the apex of the petrous bone may sometimes be seen in acoustic tumours. Dilatation of the porus acusticus indicates an acoustic tumour, but its absence is of no diagnostic significance. For operation to remove a tumour from the cerebello-pontine angle the importance of foreknowledge that there is an extension into the cave of Meckel needs no emphasis. Operation has been undertaken in only six cases. In two cases the tumour was completely and successfully removed by de Martel [1] and Guillaume [2], one by the middle fossa approach with division of the tentorium along the crest of the petrous bone, and one by the posterior approach. Both were small tumours. In the cases of Cushing [4] and Shelden [14] the removal of the tumour by the temporal approach was incomplete as the tumour occupied largely both the posterior and middle fossa. The other two reported cases [5, 12] died from the operation.

SUMMARY.

(1) Two cases of primary neurofibroma of the trigeminal nerve-root are described.

(2) Fifty-four cases of primary tumours of the trigeminal root and Gasserian ganglion reported in the literature are analysed.

(3) From this analysis there appears to be a distinction between the clinical picture of Gasserian ganglion tumours and that of trigeminal root-tumours. In Gasserian ganglion tumours continuous facial pain is the main symptom. In trigeminal root tumours facial pain is usually slight or absent and the clinical picture is one of cerebellopontine angle disorder.

(4) The symptomatology and diagnosis of trigeminal root tumours is discussed.

I desire to thank Mr. Hugh Cairns for his help in the preparation of this paper and for allowing me free access to all his material. I am also greatly indebted to Dr. Dorothy Russell for assistance in preparing the pathological section of this paper and to Dr. Russell Brain for permission to use the clinical record of Case 1.

BIBLIOGRAPHY.

A.—Primary Tumours of the Trigeminal Root.

[1] Alajouanine, Th., de Martel, Th., Oberling and Guillaume, J. *Rev. Neurol.*, 1930, **54**, 1250.
[2] Alajouanine, Th., Thurel, R., and Guillaume, J. *Ibid.*, 1935, **63**, 897.
[3] Altmann, F. *Beitr. z. path. Anat. u. z. allg. Path.*, 1928, **80**, 361 (2 cases).
[4] Cushing, H. *Amer. Journ. Med. Sci.*, 1920, **160**, 157.
[5] Giani. *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1908, **19**, 452.
[6] Gjertz and Hellerström. *Acta Med. Scand.*, 1923, **63**, H. 1-2.
[7] Glaser, M. A. *Annals of Surgery*, 1935, **101**, 146.
[8] Hagelstam. *Deutsch. Zeitschr. f. Nervenheilk.*, 1898, **13**, 205.
[9] Hellsten, M. *Ibid.*, 1914, **52**, 290.
[10] Homen. *Neurol. Centralblatt*, 1890, **9**, 385.
[11] Marie, Pierre, Bouttier, H., and Bertrand, J., *Rev. Neurol.*, 1920, **10**, 977.
[12] Nowotny, K., and Uiberall, H. *Zeitschr. f. d. ges. Neurol. und Psychiatr.*, 1934, **150**, 75.
[13] Petrina and Klebs, E. *Prager Viertelj. f. prakt. Heilkde.*, 1877, 133 and 134.
[14] Shelden, W. D. *Journ. Amer. Med. Assoc.*, 1921, **77**, 700.

B.—Primary Tumours of the Gasserian Ganglion.

[15] Blessig. *St. Petersburger med. Zeitschr.*, 1866, **10**, 65.
[16] Bradley, G., and Walton-Smith, P. E. *Med. Journ. Australia*, 1931, **18**, 1931.
[17] Cohen, J. *Journ. Nerv. and Ment. Dis.*, 1933, **78**, 492.
[18] Cooper, M. J. *Amer. Journ. Med. Sci.*, 1933, **185**, 315 (3 cases).
[19] Dercum, F. X., Keen, W. M., and Spiller, W. G. *Amer. Journ. Med. Assoc.*, 1900, **34**, 1026.
[20] Dew, H. R. *Australia and New Zealand Journ. Surg.*, 1933, **3**, 130.
[21] Frazier, Ch. H. *Amer. Journ. Med. Sci.*, 1918, **156**, 483 (3 cases).
[22] Gaines. *Med. Clinics of N. America*, 1929, **12**, 1245.
[23] Goodhart. *Trans. Path. Soc. Lond.*, 1886, **37**, 21 (2 cases).
[24] Hartmann, F. *Journ. f. Psychologie u. Neurol.*, 1905-6, **6** and **7**, 209 (2 cases).
[25] Hausch, V. *Münch. med. Wchnschr.*, 1886, **33**, 702.
[26] Hofmeister and Meyer. *Deutsche Zeitschr. f. Nervenheilk.*, 1906, **30**, 207.
[27] Krebs, M. E., Rappoport, F., and David, M. *Rev. Neurol.*, 1932, **58**, 700.
[28] Krepuska. *Monatschr. f. Ohrenhkde.*, 1898, **32**, 78.
[29] Krogius, A. *Rev. de Chir.*, 1896, **16**, 434.
[30] Learmonth, J. R., and Kernohan, J. W. *Brain*, 1930, **53**, 86.
[31] Little, T. E. *Dublin Journ. Med. Sci.*, 1873, **55**, 94.
[32] Marchand, F. *Festschr. f. Rindfleisch*, Leipzig, 1907, p. 265.
[33] Mixter, J., and Lund, Ch. C. *Arch. Neurol. and Psychiatr.*, 1936, **35**, 432.
[34] Nowotny, K., and Uiberall, H. *Zeitschr. f. d. ges. Neurol. and Psychiatr.*, 1934, **150**, 75 (2 cases).
[35] Parker, H. L. *Minnesota Med.*, 1924, **7**, 69.
[36] Rand, C. W. *Surg. Gyn. Obst.*, 1925, **40**, 49.
[37] Russell, E. C. *Journ. Amer. Med. Assoc.*, 1925, **84**, 413.

[38] Sachs, B., and Berg, A. A. *Berlin klin. Wchnschr.*, 1913, **50**, 1395.
[39] Sachs, E. *Annals of Surgery*, 1917, **66**, 152.
[40] Sheldon, W. D. *Journ. Amer. Med. Assoc.*, 1921, **77**, 700 (2 cases).
[41] Smith, R. W. "A Treatise on the Pathological Diagnosis and Treatment of Neuroma." Dublin, 1849.
[42] Söderbergh. *Nord. Med. Arkiv.*, 1909, Abt. II, H. 34.
[43] Spiller, W. *Amer. Journ. Med. Sci.*, 1908, **136**, 721.
[44] Stammers, F. A. R. *Brit. Journ. Surg.*, 1930, **18**, 125 (2 cases).
[45] Verger, H., and Grenier, H. *Rev. Neurol*, 1905, **10**, 704.

NEUROMYELITIS OPTICA.

BY BEN H. BALSER, M.D.[1]

Travelling Fellow, Department of Neurology, Montefiore Hospital, New York, N.Y.

(From the Pathological Laboratory, National Hospital, Queen Square.)

HISTORICALLY, it was Sir Clifford Allbutt [1] who, in 1870, first reported ophthalmoscopic signs associated with spinal cord disease. Using a relatively new instrument, the ophthalmoscope, he described blurring of the disc margins, slight hyperæmia, and atrophy of the disc in several cases of myelitis. He was followed in turn by Erb, Steffan, Chauval, Sequin, Noyes, Rumpf, Chisholm, Dreschfeld and Knapp. In 1889 Achard and Guinon reported the first clinico-pathological study of this disease. Then Eskridge, Drake-Brockman, Mahokian, Shanz, and Sharkey and Lawford each reported cases. Devic [2] summarized these cases in his classical "Thèse de Lyon" and this classical entity has, since then, often been referred to as "Devic's Syndrome." Reports appeared regularly thereafter in the literature of most countries and in 1927 Beck [3] made a careful review of seventy cases. Since then about forty additional cases have been reported.

This report includes the clinico-pathological studies of three cases and the clinical report of a fourth case of neuromyelitis optica. There are many cases in the literature, even to the present day, reported under this title which on analysis prove to be disseminated or diffuse sclerosis. It is intended in this report to indicate the reasons for setting apart this disease from acute disseminated and diffuse sclerosis and acute disseminated encephomyelitis, to reconsider its ætiology, and to discuss questions raised by Beck and others.

Devic called this syndrome "neuromyélite optique aiguë." Other synonyms which have appeared are acute disseminated myelitis, neuroptico-myelitis, neuromyelitis optica, diffuse myelitis, diffuse myelitis with optic neuritis, ophthalmoneuromyélite, neuropticomyélite aiguë and Devic's syndrome.

The ætiology is unknown. There are several different schools of thought. Milian, Lhermitte, Schaeffer and Horowitz considered it a

[1] Submitted as thesis for Med.Sc.D. degree, Columbia University, New York, N.Y.

virus disease and attempted to isolate the virus, but were unsuccessful. They made intracerebral and corneal scarification inoculations in dogs and monkeys with the cerebrospinal fluid of a case which they had observed. Redlich and Pette include this disease in disseminated encephalomyelitis and also believe it to be due to a filtrable virus. J. Dechaume, Von Bogaert and Vedel and Puech consider it part of the syndrome of epidemic encephalitis. Van Gehucten and Gaudissart include it in the myelitides, while Guillain and L. Michaux consider it a separate nosologic entity. In all countries there are many who consider it a form of acute disseminated sclerosis.

Report of Cases.

Case 1.—A. S., a female, aged 42, was admitted to the National Hospital, Queen Square, under Dr. Gordon Holmes on September 11, 1935. She was entirely well up to two months prior to admission when she developed marked asthenia and an aching pain, gradual in onset, down the inner aspect of both thighs and the backs of both legs. This pain spread up the back so that three weeks before admission it was present in the shoulders and neck; at that time she complained of impairment of vision in both eyes. The pain was gradually replaced by itching. The following week, her vision became worse, she became generally weak, especially in her right leg, and she now felt feverish. One week later she was admitted to the South London Hospital for Women, where examination revealed a temperature of 101° F., inequality of the pupils, the left being larger than the right, with visual acuity of $\frac{6}{60}$ in both eyes. There was rigidity of the neck. The abdominal reflexes were absent and she had bilateral extensor plantar responses. The cerebrospinal fluid was reported as being normal. At this time, urinary incontinence appeared and was followed by retention. Four days before admission her vision improved, but the following day it again became worse and she complained of photophobia. The next day she was completely blind.

On examination in the National Hospital, she lay helplessly in bed, breathing mainly with her accessory respiratory muscles. She appeared quiet and rather drowsy. She was totally blind, both optic discs being hyperæmic with blurring of the upper nasal edges. Her pupils were unequal, the left being larger than the right. There was no wasting or alteration in tone in the upper extremities, but paresis and a coarse tremor of both hands and arms were present. The lower intercostal muscles were moving poorly and she was unable to sit up. There was weakness in both lower extremities. Her abdominal reflexes could not be elicited. There was a bilateral extensor plantar response. She had analgesia to pin-prick up to the 6th dorsal segment, with a 6-in. band of hyperalgesia above this level. Cotton-wool and vibration were normally appreciated on the legs. Examination of the other systems gave negative results. The cerebrospinal fluid had a fine flocculent coagulum, 184 cells, of which 15 per cent. were polymorphonuclear leucocytes, and a total

protein of 80 mgm. per cent. The Wassermann reaction and colloidal gold curve were negative.

The illness rapidly progressed so that on September 18 she was placed in a Drinker respirator because of difficulty in breathing. Death occurred the following day.

Post-mortem examination.—There was a slight erosion of the skin over the chin and sacrum and considerable lividity of the face and neck. The brain, spinal cord, optic nerves and posterior part of the retinæ were removed. These looked normal except for an area at about the 5th and 6th dorsal segments in the cord which was shrunken and more pink than other parts of the cord. The

FIG. 1.—A. S. Section through optic nerves, chiasm, optic tracts and adjacent structures showing extensive demyelinization. Weigert-Pal counterstained with carmine.

lungs, heart, stomach and intestines were healthy. There was some cloudy swelling of the liver and early septic changes in the spleen. The pelvis of the right kidney was dilated in its upper part and its wall was hæmorrhagic and inflamed. The bladder wall was intensely congested and contained blood-stained urine.

Section from the frontal and occipital lobes, the basal ganglia, the optic nerves, chiasm, and tracts with the neighbouring diencephalic structures, the mesencephalon, pons, medulla and spinal cord were embedded in celloidin. Sections were stained by the Weigert-Pal method for myelin sheaths, the Gros-Bielschowsky method for axis cylinders, the aniline blue-orange G method for neuroglia fibres and cells, and by the Van Gieson, thionin blue and Perdrau methods.

In the white matter of the centrum ovale and in the basal ganglia, there was here and there a perivascular infiltration of lymphocytes and plasma cells

but no other changes. A section through the optic nerves, chiasm and tracts and neighbouring hypothalamus and geniculate bodies showed the severity of the pathological process (fig. 1). These sections stained with Weigert-Pal, counterstained with carmine, showed a diffuse affection of the myelin sheaths, almost complete in extent, of both optic nerves and the chiasm. The tracts, although severely involved, were almost intact in their posterior portions. Gros-Bielschowsky stains of the optic nerves showed the axis-cylinders in a state of thickening, fragmentation or end-bulb formation, or completely destroyed (Plate V, fig. 2). Despite this degree of involvement, small islands of apparently intact myelin sheaths and axis-cylinders were seen in these areas. The perivascular infiltration was marked and contained lymphocytes, polymorphonuclear leucocytes and plasma cells. The process appeared to extend into the adjoining hypothalamic structures and involved the tracts in the supra-optic, ventro-medial and posterior hypothalamic nuclei (Le Gros Clark) [7]. There was a proliferation of blood-vessels throughout these regions, more than is normally seen in this area.

FIG. 3.—A. S. Section through the cervical segments of the spinal cord showing the diffuse nature of the demyelinization. Weigert-Pal's method.

Sections made at the level of the colliculi and the level of the caudal end of the mammillary bodies, showed the same type of affection of the tracts in both bases pedunculi. There was demyelination and destruction of axis-cylinders in a totally asymmetrical fashion of parts of the fronto-pontine, pyramidal, and temporo-pontine tracts.

On examination of the spinal cord the segments C4 and 5 were most severely involved. At this level there was a complete demyelination of the cord except for the dorsal half of the posterior column. From this region upward to C2 and downward to C8, the process was a continuous one, tending to diminish in severity as it approached these limits (fig. 3). In the lumbar segments there was similar but much less extensive disease. Wallerian degeneration was present in the spino-cerebellar and spino-thalamic tracts at C1 and in the pyramidal tracts in the dorsal and lumbar segments. Throughout most of the

PLATE V.

FIG. 2.

FIG 4.

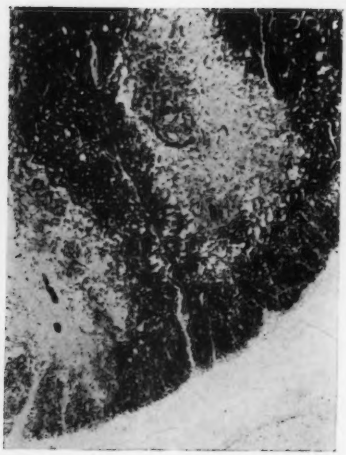

FIG. 5.

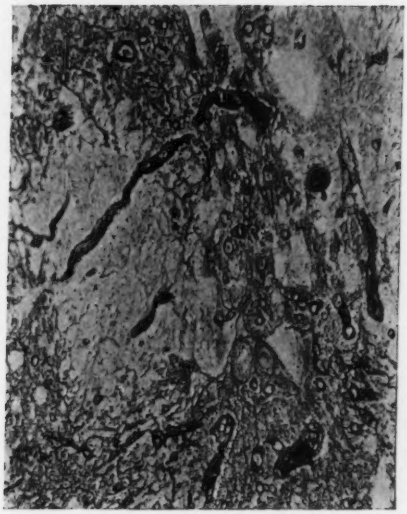

FIG. 6.

FIG. 2.—A. S. Section through optic nerves showing axis cylinders in a state of thickening, fragmentation or end-bulb formation, or completely destroyed. Gros-Bielschowsky counterstained with Van Gieson.

FIG. 4.—E. A. Section through the optic tracts showing early lesions in centre of right optic tract with perivascular destruction of axis cylinders. Gros-Bielschowsky's method counterstained with thionin blue.

FIG. 5.—E. A. Section through spinal cord at D9 showing cavity formation. Weil's method.

FIG. 6.—A. B. Section through spinal cord at C8 to show intense fibroplastic overgrowth. Perdrau's method.

To illustrate paper by Ben H. Balser.

demyelinated areas, there could be found many intact single sheaths. There was a perivascular infiltration of lymphocytes, plasma, and endothelial cells, throughout the cord and meninges, while in the cervical region polymorphonuclear cells were also present. In the more affected areas there was a proliferation of blood-vessels, but very little connective tissue. Thickening and end-bulb formation of the axis-cylinders was seen in the demyelinated areas of the cervical cord, but here again many of them were intact. There was very little glial fibre proliferation in any of the affected areas.

Case 2.—E. A., female, aged 50, was admitted to the National Hospital under Dr. E. A. Carmichael on March 9, 1935. She was perfectly well up to November, 1934, when she developed severe pain in the back associated with high fever and sweating. After three weeks in bed, she got up but had recurrence of the pain and temperature. A surgeon was called in at this time and he operated on her for a growth (?) of the right kidney which he removed. Improvement was slow thereafter, and five weeks later she was just able to get about by holding on to objects in the room. Three weeks later (four weeks prior to admission) she had a sharp, sudden pain in the right inguinal fossa, just above and parallel to Poupart's ligament. The pain would come every hour or so for a few seconds, and lasted about four days. Then, after a three-day interval there was a four-day period of intermittent hiccough, lasting thirty to sixty seconds at one to two-hour intervals. This also disappeared spontaneously. After another three-day interval, there followed a four-day period of retching, which occurred two or three times daily. There was no vomiting. Again followed a three-day interval of well-being. The patient then developed numbness in both feet, greater on the left than on the right, which slowly spread up the left leg to the buttock and groin, and up the left leg to the knee. Three days later (four days prior to admission), she was unable to stand alone because of weakness in both legs. At this time, numbness and weakness of the left hand and forearm appeared and spread rapidly up the arm. The following day she was unable to feel the passing of fæces or urine, but had a normal call to stool.

On examination in hospital the patient was a grey-haired, very thin, elderly woman, showing marked general wasting of subcutaneous fat of the limbs and trunk. Her mentality was unimpaired. The visual acuity, both right and left, was $\frac{6}{9}$, the fields were full to confrontation tests and the fundi appeared normal. There were no abnormalities of the other cranial nerves. The upper limbs were thin, but there was no localized muscular wasting and power was apparently normal in all muscle groups except the extensors of the left forearm. Tone was normal. There was no disturbance of co-ordination. She was unable to sit up without using her arms. Both lower extremities were thin with generalized subcutaneous wasting. Tone was slightly increased on both sides, and there was impairment of power in flexion and extension at the left ankle. Co-ordination was poor on both sides. All the tendon reflexes were increased and the abdominal reflexes were absent. There were bilateral extensor plantar responses. Complete loss to all forms of sensation

was present up to the level of L1, with no sensory disturbance above this level. Examination of the other systems showed no abnormality except for the nephrectomy scar in the right loin. The spinal fluid protein was 110 mgm. per cent. and it contained 38 cells. The Wassermann reaction and colloidal gold curve was negative. The blood showed a leucocytosis of 12,200, of which 85·5 per cent. were polymorphonuclear cells.

Progress.—The patient rapidly became weaker. On March 17 the edges of both optic discs were blurred, but there was no gross visual defect. The weakness and sensory disturbance progressed so that examination on April 6 showed marked wasting of both upper limbs, more on the left than on the right, with moderate weakness of the left arm. Tone was diminished on both sides. There was a questionable sensory level to pin-prick at C2. Appreciation of vibration was present in both upper extremities, but position-sense was greatly diminished in the fingers of the left hand, though not of the right. Appreciation of size, shape, form and weight of objects, and two point discrimination were greatly disturbed in the left hand.

Her condition rapidly became worse, and she died on April 20.

Post-mortem examination.—The brain and cord were removed. There was a diffuse softening of the cord throughout the lower thoracic and lumbar enlargement, without much shrinkage. The lungs, liver, and spleen were normal. The heart was small and pale, with rather thin ventricular walls. The vessels of the heart were normal, but the mitral valve showed a marked thickening and dilatation of one cusp. The right kidney was absent, and the left showed slight inflammation in the pelvis. The bladder contained thick purulent urine.

As in the preceding case, pieces taken from the frontal and occipital lobes, the basal ganglia, through the optic chiasm and tracts with the neighbouring diencephalic structures, through the mesencephalon at its uppermost and lowest levels, and from the different segments and of the spinal cord were embedded in celloidin. These sections were stained by the Weil method for myelin sheaths, the Gros-Bielschowsky method for axis-cylinders counter-stained with thionin-blue, the Mallory phosphotungstic acid hematoxylin method for neuroglia fibres and cells, and by the Van Gieson, Scharlach R and Perdrau methods.

The sections of the occipital and frontal cortex and the basal ganglia showed perivascular infiltration with lymphocytes and plasma cells. This was not very marked in degree or extent, but was definitely pathological. The occipital lobe and basal ganglia showed more involvement than the frontal lobe. Here the myelin sheaths tended to be crowded away by the dilated perivascular spaces, but there was no evidence of perivascular demyelination in these areas.

Serial sections were made through the optic tracts. In the centre of the right optic tract was a fairly large area of destruction of myelin sheaths and axis cylinders (Plate V, fig. 4), with a cellular infiltration of lymphocytes, plasma and endothelial cells. Polymorphonuclear cells were occasionally seen. Scattered

throughout both optic tracts were smaller areas of perivascular demyelination and axis cylinder destruction which accompanied areas of perivascular infiltration containing the same type of cells as previously described. This infiltration was marked in the chiasm. Occasional intact myelin sheaths and axis cylinders were noticeable in each involved area. There was no glial fibre proliferation.

Sections through the upper and lower levels of the mesencephalon showed a more severe affection of the tracts of both bases pedunculi, but again in an asymmetrical fashion. There was demyelination, axis cylinder destruction, and beginning cavity formation. There was no glial or connective tissue reaction.

On examination of sections of the spinal cord, two areas of involvement with a relatively unaffected area between them were found. The upper and more severe affection was at C4 and C5, gradually diminishing in intensity toward C2 and C8. The lower was most severe at D6, diminishing in intensity up to D3 and down to L2. The area between, from C8 to D3, was intact except for Wallerian degeneration of the spino-cerebellar and spino-thalamic tracts. The region below L2 was also intact, except for Wallerian degeneration in the pyramidal tracts. A cavity formation was found at D9 (Plate V, fig. 5). The lower area was more severely involved than the upper, the cord being completely demyelinated at D6. Throughout the diseased areas occasional intact myelin sheaths and axis cylinders were seen. The axis cylinders were destroyed in the regions above described. Proliferation of blood-vessels was quite marked and was present even in what appeared to be unaffected areas. There was an intense perivascular infiltration of lymphocytes, plasma cells, and occasional polymorphonuclear cells, throughout the cord. There was very little proliferation of neuroglia fibres or connective tissue. Occasional giant astrocytes were seen in the proximity of engorged blood-vessels in the less affected areas.

Case 3.—A. B., female, aged 15, came under the care of Dr. C. P. Symonds on May 10, 1930. She was well up to January, 1929, when she contracted influenza which left her feeling generally weak. In July, 1929, while walking, she fell down and found her right leg numb and useless. The numbness rapidly disappeared, but the weakness in the right leg remained for three weeks and then cleared up. In September, 1929, she began to drag her left leg and again fell down a few days later. This time her left leg felt numb and useless. After three weeks in bed the right leg also became useless but both recovered by December. In January, 1930, she again dragged her right foot and fourteen days later her left foot. At this time the fingers of her left hand became weak and her vision became so badly affected that she was totally blind in her left eye in three or four days. Power in her legs and vision improved, but she could not fully extend the fingers of her left hand.

Examination.—On May 14, 1930, she had a visual acuity of $\frac{6}{18}$ on the right and $\frac{6}{24}$ on the left. There was a generalized constriction of both peripheral fields with a paracentral scotoma in the upper field of the left

eye. There was pallor of the left disc. The left pupil failed to hold its contraction to light. The interoseii of the left hand were wasted, but there was no alteration in tone in the upper extremities. Power here was good and equal, except in the left hand where the grip was very weak and the fingers could not be extended or thumb adducted. There was a coarse tremor of the extended fingers. The muscles of the trunk and lower extremities were all wasted in a symmetrical fashion and tone was diminished. Power in the trunk and legs was greatly impaired, the left leg being more affected than the right, and more distally than proximally. The tendon reflexes were absent in the left upper and both lower limbs, but were very active in the right upper limb. The abdominal reflexes were absent. There was a complete loss of sensation to cotton-wool and pin-prick below D2 on the right and D4 on the left. Position sense and appreciation of vibration were intact in the upper extremities but absent in the lower. Her physical examination was otherwise normal. The cerebrospinal fluid contained 15 cells and 40 mgm. per cent. of protein. The Wassermann reaction and colloidal gold curve were negative.

She slowly and progressively became worse thereafter, and died in March, 1931.

Post-mortem examination.—Only the spinal cord was received for examination. It showed no gross abnormalities on naked eye inspection. Segmental sections were embedded in celloidin and stained by the Loyez, Aniline Blue-Orange G, Phosphotungstic Acid Hemotoxylin, Perdrau and Van Gieson methods.

A diffuse demyelinating process was present in the cervical and dorsal region. It was most severe from C8 to D4, decreasing in intensity down to D10 and going up as far as C4. In the region from C8 to D4, the entire cord was involved, yet occasional bundles of intact myelin sheaths could readily be seen. Below D10 both the pyramidal tracts showed Wallerian degeneration. In all of the affected areas there was a proliferation of smaller blood-vessels. The perivascular infiltration consisted of lymphocytes, plasma, and endothelial cells with occasional polymorphonuclear leucocytes. In the lumbar segments, the infiltration was greatest in the region of the anterior horns. There was very little glial tissue reaction. There was an intense fibroblastic overgrowth in the dorsal columns at C8 and D1, which gradually lessened in degree toward C6 and D4 (Plate V, fig. 6). Such a reaction was not seen in Cases 1 and 2. It was greatest around the blood-vessels and seemed to spread out from them.

Case 4.—M. K., a girl, aged 11 years, was admitted to the National Hospital under Dr. George Riddoch on March 13, 1935. She was well up to the beginning of 1933 when, during the first three months of that year, she developed consecutive attacks of acute nephritis, measles and whooping-cough. At the end of May, 1933, she returned home from school, complaining of general malaise, pain in the back, a cold and shivery feeling. She was restless that night, but the following day seemed to have recovered completely. After remaining in bed for three weeks she was allowed to be up, and one afternoon

complained that her vision was blurred. This progressed rapidly so that two days later blindness was complete, apparently even to light perception. There were no other complaints. Blindness remained for about a week when the vision began to improve rapidly, so that by the early part of August it seemed to be quite normal (approximately five weeks after the onset of the blindness). Vision remained good for about six weeks, but in the early part of September there was a relapse. Vision again failed to such an extent that the patient could not see to read. The right eye was more affected than the left, and was, in fact, almost completely blind. She remained well, except for the visual defect, until the last week of February, 1935, when she came home from school one afternoon complaining of pain in both elbows and in the back, high up between the shoulder blades. After a week in bed these complaints cleared up, but on arising she was found to be more weak and unsteady than could be accounted for by the week in bed. She fell once or twice, from unsteadiness rather than weakness, and tended to stagger on walking.

Examination.—She was a thin but fairly well-developed girl, bright, alert and attentive. The right eye was blind even to light perception, but with the left eye counting fingers was possible at two feet. Both optic discs were clearly defined but paper-white in colour, the right more than the left. The physiological cups, vessels, maculæ and the retinæ showed no abnormalities. The visual field of the left eye showed a general constriction with a central scotoma. Convergence was poor, fixation being attempted with the left eye. The pupils were of normal size, equal and round, the right immobile to direct light but reacting consensually, the left reacting briskly to light and on convergence but failing to maintain the contraction. The lower extremities were both a little wasted. There was paresis of the flexors of the hip only. There was unsteadiness in heel-shin-finger tests but no gross ataxia. All the tendon-jerks were active, the knee and ankle jerks much more than the others. Only the right upper abdominal reflex could be elicited and the response was easily exhausted. There were bilateral extensor plantar responses, A sensory level to pin-prick and heat and cold, was present at D5-6, with a slight diminution in appreciation of cotton-wool stimuli as well. Appreciation of vibration was impaired in both lower extremities but position sense was intact. Her general physical examination was otherwise normal.

Progress.—She improved in hospital. The ataxia completely cleared up, the abdominal reflexes returned and the plantar responses became doubtfully flexor. The sensory level, although still definite, was nevertheless diminished. Her vision remained unchanged. She was discharged on March 29, 1935.

Discussion.

Clinical diagnosis. — In differentiating neuromyelitis optica from acute disseminated sclerosis, it is known that the former disease may occur at any age, many cases being reported in children of 10 years, or even less. Disturbances of vision are dramatic, being bilateral and often progressing rapidly to complete blindness. The blindness may

develop in the course of a few days with or without remissions and relapses. When remissions occur, careful examination usually shows permanent damage in the form of diminution of visual acuity, or scotomata. The visual disturbance may precede or follow the myelitic process. In those cases in which the spinal cord is involved before the optic pathways, the sensory disturbances are of primary importance. The occurrence of pain in the extremities and in the back, with a gradually ascending numbness in the extremities up to a distinct level, frequently in the lower cervical region, is a common mode of onset. This sometimes leads to an erroneous clinical diagnosis of spinal neoplasm. There is no mental disturbance, and involvement of the other cranial nerves, other than the optic, or of the cerebellum practically never occurs. Remissions in the disease as a whole, may or may not occur (Beck 10 per cent., Perritt 50 per cent.), and relapses are infrequent. Contrasted with this, disseminated sclerosis is a condition which occurs at puberty or later and which often involves vision in one eye but rarely in both eyes. Pain is an infrequent complaint but numbness is quite common. However, both these symptoms, when they present themselves, are usually localized and not progressive.

The post-infections and post-vaccinial acute disseminated encephalomyelitis can be differentiated more easily from neuromyelitis optica. This syndrome is frequently initiated by pain in the extremities and in the back and progressive numbness which usually does not stop at a level. The ataxia, disturbance of co-ordination and severe mental symptoms dominate the clinical picture. Differentiation is aided also by the history of preceding infection or vaccination, and the lack of involvement of the visual pathways in disseminated encephalo-myelitis.

Cerebrospinal fluid.—In neuromyelitis optica there may be an increase in polymorphonuclear cells in the cerebrospinal fluid. The colloidal gold curve is negative. In this disease there may be also a relative or absolute increase in polymorphonuclear cells in the blood. In disseminated sclerosis, if pleocytosis of the cerebrospinal fluid is present, there are few, if any, polymorphonuclear cells, and changes in the celloidal gold curve, of the paretic type, occur in about 25 per cent. of cases (H. H. Merritt). In both diseases the spinal fluid protein may or may not be increased and this determination is of no value in differentiation.

Pathological diagnosis.—Neuromyelitis optica, as summarized from the cases herein reported, is characterized by an asymmetrical diffuse demyelination of the cord, brain-stem, and optic nerves and tracts.

From the study of early lesions of the optic tracts (serial sections in Case 2), it appears that the lesions are perivascular and may be in the centre of the tracts at first, and extend or coalesce so that there soon appears a central core of destruction of myelin sheaths and axis cylinders. This, in many instances, may not occur. The process in the spinal cord tends to be continuous in nature, rather than spotty, and islands of intact myelin sheaths or isolated sheaths are present in affected areas, in which regions cavity formation also may be found. The axis cylinders show thickening, fragmentation, and end-bulb formation, although many of them may be entirely intact. There is a considerable proliferation of blood-vessels and a perivascular infiltration consisting predominantly of lymphocytes and plasma cells. Polymorphonuclear leucocytes can also be demonstrated in some of the involved areas. Only occasionally increase in glial cells is seen. This perivascular infiltration may be found to be present throughout the central nervous system to a greater or lesser degree. Occasional giant astrocytes are seen in the proximity of an engorged blood-vessel or capillary. There is only a slight, if any, proliferation of neuroglial fibres and connective tissue, at least in the early acute non-remissive stage. However, a dense fibrous tissue overgrowth may occur later in the disease and may be seen extending from the infiltrated blood-vessels (Case 3).

Contrasted with this pathological picture, in acute disseminated sclerosis the demyelinated areas are usually "punched out" in appearance rather than infiltrating at their borders, with complete destruction of all myelin sheaths within the involved areas, whereas there are always small bundles of intact myelin sheaths in neuromyelitis optica. The axis cylinders are usually intact. The involved areas may be asymmetrical, but are not continuous as in neuromyelitis optica, and cavity formation does not occur. Polymorphonuclear cells are not seen, the perivascular infiltration which is present being composed chiefly of lymphocytes and plasma cells with some compound granular corpuscles. There is an abundance of neuroglial fibres and cells. Any part of the central nervous system may be affected.

Pathologically, acute disseminated encephalomyelitis is an asymmetrical diffuse demyelinating disease which is distinctly perivascular in nature. Throughout the white matter of the brain and brain-stem, the sub-ependymal zones, and the marginal zones of the spinal cord may be seen small discrete areas of myelin sheath and axis cylinder destruction, varying in size, but not coalescing as in neuromyelitis optica. Simultaneously, with or without demyelination, there is a

perivascular gliosis consisting of microglia and a perivascular infiltration consisting of lymphocytes and plasma cells, but polymorphonuclear leucocytes are not present.

The pathological process in diffuse sclerosis resembles that of neuromyelitis optica. The optic nerves and tracts may show changes, the early lesions in them being similar to those in neuromyelitis optica. That is, there is a perivascular myelin sheath and axis cylinder destruction lying centrally in the tracts, and tending to produce a central core of destruction (Alfred Meyer). The demyelination of the centrum ovale is diffuse in nature, the axis cylinders being involved, sometimes to complete destruction. Early in the disease the perivascular infiltration may be slight, but soon increases in severity and is composed of lymphocytes, plasma and gitter cells. Large globoid and multinucleated giant cells found at the periphery of the lesions have been described (Stewart, Greenfield and Blandy [4]), but these are not seen in neuromyelitis optica. With progression of the disease there is a moderate proliferation of connective tissue and neuroglial fibres in the affected areas. Large giant astrocytes are occasionally seen. Wallerian degeneration is usually present.

In the Withering lectures of 1935, Weston Hurst [6] has pointed out that the perivascular infiltration found in the central nervous system in virus diseases is a reactive phenomenon; that the neurotropic viruses are essentially cytotropic in their affinity; and that there is no known virus disease of human beings in which the virus will produce demyelination on injection into susceptible animals. On the other hand, the perivascular nature of the myelin sheath and axis cylinder destruction, with an increase in polymorphonuclear cells in both blood and spinal fluid, and their presence in the perineural and perivascular spaces, would speak for a toxic or infectious process in the blood stream which has, apparently, an affinity for the central nervous system. For the present, therefore, it does not seem likely that neuromyelitis optica is due to a virus. The field of study of virus diseases and their pathogenicity is relatively new, and with more study of the demyelinating diseases, it is possible that a virus may be isolated and proved to be the ætiological factor in neuromyelitis optica.

Beck had indicated that 35 per cent. of the cases he reviewed consisted of disseminated foci, while in the remaining 65 per cent. there was a diffuse myelitis varying in extent from three segments to an involvement of all of the thoracic and many of both the lumbar and cervical segments. He considered that "it is possible that these two

types represent two distinct diseases with a common clinical picture." Cases 1 and 2 herein reported are "disseminated" in the sense that there are at least three separate areas of involvement. In Case 1 most of the cervical and some of the lumbar segments are involved, with complete sparing of the dorsal segments. The brain stem is also involved. In Case 2 the segments from C2 to C8 were affected with a clear area, except for Wallerian degeneration, from C8 to D3, and the remaining dorsal segments are severely affected. Here again the brain stem was involved. Case 3 represents the "diffuse" type, since there is one continuous involvement from C4 to D10. Except for this difference in distribution of the lesions, the pathology is exactly the same in all three cases. Since the clinical picture is the same in all cases, it does not seem justifiable to assume a difference in diseases on the basis of distribution alone, unless by the term "disseminated," Beck had intended many small foci in the cord with some differences in the clinical and pathological studies.

Remissions in a disease with such severe pathology are surprising. It might be assumed, however, that the very rapid clinical changes are due, in a large measure, to an extensive reactive process which interferes with physiological function. Although reports are made of complete recovery of function in both optic nerve and cord, there may well be some permanent damage which remains so small as not to be readily detected.

(The author wishes to express his appreciation and thanks to Dr. J. Godwin Greenfield for his constructive criticism of this work, and to Drs. Gordon Holmes, E. Arnold Carmichael, C. P. Symonds and George Riddoch for permission to use the cases herein reported.)

BIBLIOGRAPHY.

[1] Allbutt, T. C. "On the Ophthalmoscopic Signs of Spinal Disease. *Lancet*, 1870, **1**, 203.
[2] Devic, C. *Thèse de Lyon*, 1894. Congrès français de medicin, 1894, **i**, 139.
[3] Beck, G. M. "Diffuse Myelitis with Optic Neuritis," *Brain*, 1927, **50**, 687.
[4] Stewart, T. G., Greenfield, J. G., and Blandy, M. A. "Encephalitis Periaxialis Diffusa," *Ibid.*, 1927, **50**, 1.
[5] Symonds, C. P. "The Pathological Anatomy of Disseminated Sclerosis," *Ibid.*, 1924, **47**, 36.
[6] Hurst, E. Weston. "The Neurotropic Virus Diseases," *Lancet*, 1935, **ii**, 697.
[7] Le Gros Clark, W. E. "The Topography and Homologies of the Hypothalamic Nuclei in Man," *Journ. Anat.*, 1936, **70**, 203.

THE SIGNIFICANCE OF INDIVIDUAL DIFFERENCES IN THE BERGER RHYTHM.

BY FREDERICK LEMERE.

MANY investigators [1, 2, 3, 4, 5] working on the electrical potentials of the human cortex have noticed that individuals differ in the facility with which these potentials may be obtained. Some subjects could be counted on to produce good rhythmic waves under favourable circumstances, while others never seemed to be able to give a satisfactory rhythm under any condition. The ability or inability to produce a strong Berger rhythm, therefore, seems to be an individual characteristic which it will be the purpose of this paper to investigate more thoroughly. To begin with, the Berger rhythm was studied in twenty-six normal subjects. In order to determine the degree of variation of the rhythm in any one given individual, from three to five electro-encephalograms were obtained from each subject within a period of a month or less.

The electrical potentials emanating from the brain were picked up by moist pad electrodes which were 2 cm. in diameter and were soaked in saline solution before being applied to the scalp. One electrode was usually placed on the forehead and the other on the occiput.

The amplifying unit consisted of a five stage condenser-coupled amplifier with a balanced (push-pull) input stage as described by Matthews [6]. This latter feature was very useful in balancing out extraneous electrical disturbances. The recording unit was a Matthews' ink-writing oscillograph. For the purposes of comparison, the amplification was kept constant within narrow limits.

The subjects were examined lying down in a quiet room with instructions to relax as much as possible both mentally and physically. Although Berger [7] has emphasized the importance of complete exclusion of outside stimuli in his criticisms of other worker's results, control experiments did not seem to bear this out. Some of the patients in this series were tested on a busy, noisy, open ward and subsequently in a quiet darkened room with no difference in the rhythms produced.

THE BERGER RHYTHM IN NORMAL SUBJECTS.

The most obvious rhythm was that of the alpha (10 per second) waves of Berger. As Adrian [1 and 8] and his co-workers have shown, these waves arise, for the most part, from the visual cortex, and were

usually present only with the eyes shut. Alpha waves with the eyes open were observed in only two subjects and then to a much less degree than with the eyes shut [1]. It is recognized that a 10 per second rhythm may arise in other parts of the brain than the visual cortex [9], but such extraneous "alpha" waves have little bearing on the present investigation. With the leads and method used, these waves are in-

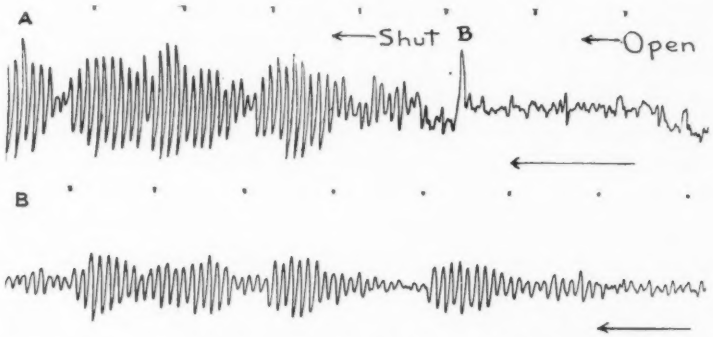

FIG. 1.—Representative sections of records from a subject with a "good" Berger rhythm. Time in seconds. A, normal record with subject relaxed mentally and physically, eyes shut at B. B, record obtained during the same trial as A but with eyes shut and carrying on a light conversation. The alpha (10 per second) waves begin as soon as the eyes are closed.

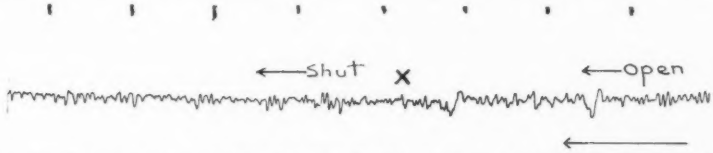

FIG. 2.—Representative section of a record obtained from a subject showing almost no alpha (10 per second) waves, but "good" beta (20 per second) waves. Eyes shut at X. Time in seconds.

significant when compared with those coming from the visual cortex with the eyes closed.

For the purpose of comparison, the alpha rhythm was classified on the basis of its amplitude, regularity, and constancy. A record was considered to show a "good" rhythm when the alpha waves were of above average amplitude (usually over 0·05 millivolts), constancy, and regularity (fig. 1). A "poor" rhythm (fig. 2) was expressed by irregular and inconstant alpha waves of low amplitude (usually less than 0·05 millivolts). The amplitude of the alpha waves was judged not only by

[1] These two subjects, producing occasional groups of alpha waves with eyes open, showed strong constant 10 per second waves with eyes open or shut when a bifrontal lead was used.

their height but also in relation to the amplitude of the irregularities of the base line. These irregularities were partly due to the primary "noise" of the apparatus (fig. 3) and partly to the complex potentials

FIG. 3.—Base line produced by apparatus alone with 5,000 ohms resistance across the electrodes.

from the brain, other than those causing the alpha waves. As such, the base line with the eyes open served as a measure both of the sensitivity of the apparatus and also of the general electrical activity of the brain as opposed to that of the occipital cortex.

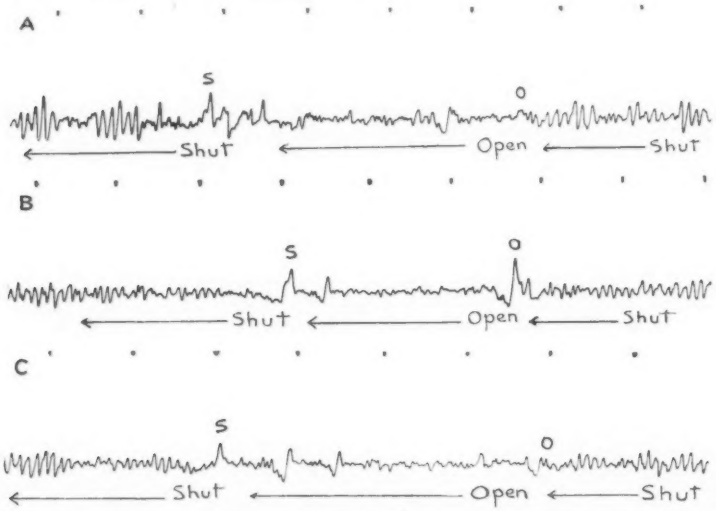

FIG. 4.—Representative sections of records from the same subject at different times. Time in seconds. Eyes opened at O and shut at S. A, first trial. B, third trial, waves not quite as "good" as in A although subject more relaxed. Shows the usual tendency for the waves to get slightly "worse" on subsequent trials. C, fourth trial, one week after B and during examinations. "Keyed up" but not worried. Less relaxed than in B.

The number of subjects showing "good" waves was about equal to that showing "poor" waves. In any one subject, there was a remarkable similarity between the records taken at different times. Only four gave "good" waves at one time and "poor" waves at another time. Of these, two gave "poor" waves in relation to a state of acute anxiety (a secret engagement and an important Rugby match).

There was a definite tendency for the alpha waves to become slightly "poorer" on subsequent trials (fig. 4, A and B). The time of the day when examined, the spacing of the trials, the mood, or the degree of tiredness could not be correlated with any changes in the waves.

The rate of the rhythm was also remarkably constant even in different subjects. In this series, the rhythm of the alpha waves was never faster than 12 per second or slower than 9 per second. Only five showed a change in rate at different trials and this did not vary more than one beat a second from the usual rate for that subject. There was no correlation between the size of the alpha waves and their rate.

As others have observed, difficult mental effort or disturbing external stimuli have a tendency to lower the alpha waves. On the other hand, in this series, an individual showing "good" waves continued to do so even when disturbed by being asked to carry on a conversation (fig. 1, B).

Berger's beta waves, those with a rhythm of from 20-40 per second, are less well understood. They were present with the eyes open or shut and seemed to be the strongest in those subjects having "poor" alpha waves (fig. 2).

The Significance of Individual Differences in Berger Rhythm.

The first question that arises is whether a quantitative comparison of the rhythms in different individuals is valid. May not physical factors, such as the thickness of the skull or the resistance of the scalp, determine whether an individual has "good" or "poor" waves? The main objection to a physical explanation of individual differences is the variability of the waves even in the same record. The variation in the regularity and size of the waves produced by drugs [2], psychological factors, and the tendency for the alpha waves to decline on subsequent trials are all more easily explained on a physiological than on a physical basis. One would expect the physical factors to remain rather constant.

The resistance between the electrodes was measured in a number of subjects during the recording of the Berger rhythm and no correlation found between "good" or "poor" waves and the inter-electrode resistance. The resistance through the dura and skull was also measured in several cadavers and found to be between 900 and 1,100 ohms, a variation inadequate to explain the differences in rhythm that would undoubtedly have been observed during life.

An even more significant bit of evidence against a physical explanation of the individual differences in Berger rhythm is that obtained

from patients with unilateral diagnostic trephine openings in the occipito-parietal region. Three such patients, who subsequently were found to have no cerebral lesions, were available. Leads from the trephined side showed waves of somewhat greater amplitude, but no greater regularity or constancy than those from the normal side (fig. 5). Even then, the differences were much less than those between persons showing "good" and "poor" waves.

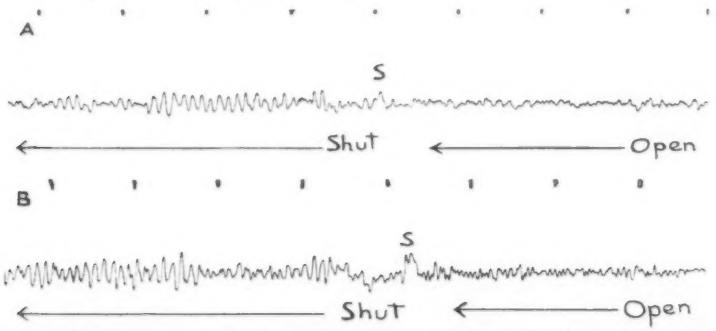

FIG. 5. Representative sections of records from a patient with a diagnostic right-sided occipito-parietal trephine. Subsequently proven not to have any cerebral lesion. A, record from left (normal) side of the head. B, record from right (trephined) side of the head. Occipital electrode over trephine. Time in seconds. Eyes shut at S.

Could not these individual differences be explained by differences in the ability to relax? Again the results did not bear this out. Several reliable subjects stated that they were most tense and had the greatest difficulty in keeping from thinking during the trial that showed the "best" alpha waves. There was also a general tendency for the waves to get "worse" with subsequent trials although relaxation became better. Ten of the subjects had examinations during the week of their last trial. There was no change in seven, but three showed "better" waves during this week (fig. 4, C). Significantly, these three stated that although they were "keyed up" they were not worried about the examinations. This suggests that a general feeling of tension may make the waves "better," but that worry or anxiety may neutralize this effect.

Another mental characteristic that one might expect in people showing "good" waves would be the ability to concentrate, so to speak, on thinking of nothing. Those showing "good" waves did seem to have good powers of concentration in general, but often stated that thoughts were flying through their mind even when the record showed a strong Berger rhythm. On the other hand, subjects with "poor" waves were

able to completely banish all conscious activity with no improvement in the Berger rhythm.

The most interesting question of all is whether there are any obvious personality differences between those having "good" and those having "poor" waves. The physical make-up, sex, intelligence, memory capacity, introversion or extroversion, and auditory or visual memory, suggested themselves as possible differentiating points but no correlation could be found between these and the ability or inability to produce alpha waves. Although no special psychological or personality tests were given to these subjects, most of them were questioned from a psychiatric point of view. My impression was that "good" waves were produced in general by the cyclothymic or manic-depressive type of individual while schizoid personalities gave "poor" waves as a rule. It was, therefore, decided to test this theory out in psychotic patients.

The Berger Rhythm in Psychotic Patients.

Electro-encephalograms were obtained from forty psychotic patients using the same procedure as for the normal subjects. Only patients who could co-operate and in whom the diagnosis was fairly clear were examined. It was soon found that senile, arteriosclerotic, or deteriorated patients had to be excluded from the group used for analysis as such processes usually seemed to preclude the production of a "good" alpha rhythm. In other words, the manic-depressive changes occurring in involutional or pre-senile cases could not properly be used in this investigation in judging as to whether a patient had a schizoid or a cyclothymic make-up. However, when young patients in a mild or

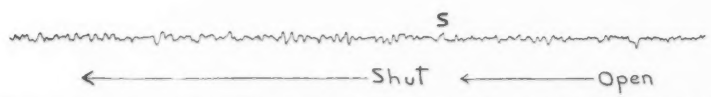

Fig. 6.—Representative section of a record taken in a patient with simple schizophrenia. Apparently normal at time the record was taken but gave history of attacks of marked apathy with feelings of unreality and reference.

recovered stage of their illness were examined, a marked difference was found in the waves produced by the two groups. Consistently "good" waves were given only by the manic-depressive patients. Schizophrenic patients, on the other hand, rarely gave "good" waves (fig. 6) and then never consistently and only when they seemed to be stimulated by such

things as visits from relatives or changes in their ward routine. It seemed that the apathy and affective deficiency of the schizophrenic was the feature of the illness most clearly related to an absent or "poor" alpha rhythm. The difference in the two groups could not be accounted for by different abilities to relax as the hypomanic patients (fig. 7) gave

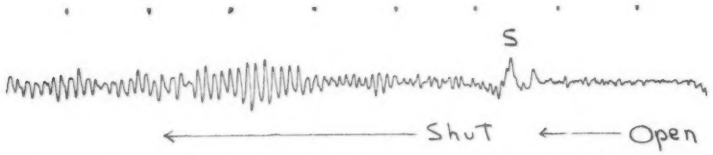

FIG. 7.—Representative section of a record taken in a patient in the hypomanic stage of a manic-depressive illness.

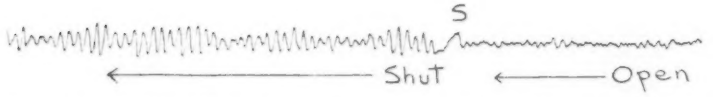

FIG. 8. Representative section of a record taken in a patient in the depressed phase of a manic-depressive illness.

just as good waves as the depressed patients (fig. 8) who were completely relaxed. Nor was the difference one of mental activity for, as nearly as could be told, the manic patients were full of ideas while the depressed and simple schizophrenic patients seemed to be able to keep from thinking too much during the tests. Fortunately, at this time I had access to a group of disseminated sclerosis patients who were being examined in detail as to their emotional and intellectual capacities. This was being done in relation to the emotional instability that is frequently a symptom of this illness [1].

THE BERGER RHYTHM IN DISSEMINATED SCLEROSIS.

Electro-encephalograms were taken by the usual procedure in eighteen cases of disseminated sclerosis. The records from five of these patients had to be disregarded as again there were signs of mental deterioration that invalidated the findings. Of the remaining thirteen patients, six complained of emotional instability as an early and trouble-

[1] I wish to thank Drs. Frank Braceland and Jack Griffin who were doing this work, and who were kind enough to allow me to go over their notes on these patients.

some symptom. Five of these six patients had "good" Berger rhythms (fig. 9) in contrast to the remainder of the group who had average or "poor" rhythms (fig. 10).

According to current psychiatric concepts, emotional lability is probably due to the uncontrolled expression of an underlying cyclothymic personality. If this is true, then a "good" rhythm is again

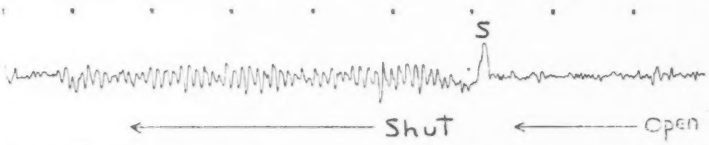

FIG. 9.—Representative section of a record obtained from a patient with disseminated sclerosis and who complained of emotional lability as an early and pronounced symptom. Shows a "good" Berger rhythm.

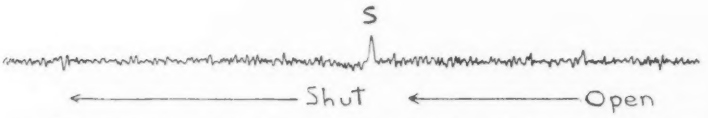

FIG. 10.—Representative section of record from a patient with disseminated sclerosis in whom there was no emotional lability. There is almost no Berger rhythm.

associated with an innate capacity for affective expression. At any rate, excluding the cases showing mental deterioration, there was a definite and close relationship between a "good" Berger rhythm and the symptom of emotional lability.

SUMMARY AND CONCLUSIONS.

From three to five separate electro-encephalograms were obtained at varying intervals from twenty-six normal adults. The object was to compare the Berger rhythm in different individuals and also in the same individual at different times.

The cerebral potentials were picked up from the scalp by moist pad electrodes. A balanced input amplifier was used in conjunction with an ink-writing oscillograph. Subjects were examined lying down, in a quiet room, and in as relaxed a state as possible.

The most obvious rhythm was that produced by the alpha waves (the 10 per second potentials from the visual cortex when the eyes are shut). Some subjects produced "good" alpha waves of relatively high regularity and amplitude (usually over 0·05 millivolts). In others, the

waves were "poor," being irregularly present and of low amplitude (usually under 0·05 millivolts).

In any one subject, the ability or inability to produce "good" alpha waves remained remarkably constant. There was a slight tendency, however, for the waves to become "worse" on subsequent trials. Moderate disturbances, such as the noise of an open ward, had little effect on the waves as long as the subject lay quietly with his eyes closed.

The rate of the alpha waves varied between 9 and 12 per second in different subjects but never more than one beat per second in the same subject. There was no correlation between the rate and quality of the alpha waves.

Faster, beta rhythms (18 to 35 per second) of low amplitude were observed with the eyes open or shut. In general, they were the most obvious in those individuals with "poor" alpha waves.

Neither the time of day when examined, the spacing of the trials, the mood, the degree of tiredness, the physical type of the subject, the sex, the intelligence, nor the type of memory, auditory or visual, seemed to matter in the production of the alpha waves. Physical factors, such as the thickness of the skull, probably have little to do with individual differences in the Berger rhythms. As long as the subject co-operated in trying to relax, his ability or inability to do so seemed to have little effect on the quality of the waves produced.

The ability to produce "good" alpha waves seems to be a neurophysiological characteristic which is related in some way to the affective capacity of the individual.

Mildly manic or depressed patients give a "good" Berger rhythm provided that there are no associated presenile or arteriosclerotic changes or signs of mental deterioration. Schizophrenic patients nearly always give a "poor" rhythm. Normal individuals with cyclothymic or schizoid personalities show the same differences.

The close relationship of "good" waves to affective capacity is further suggested by the findings in patients with disseminated sclerosis. In these patients, those exhibiting emotional instability as an early symptom usually showed much better waves than those not troubled with this symptom.

This work was financed by a Rockefeller Foundation Grant and was carried out in the Physiological Laboratories, Cambridge; the Cambridgeshire Mental Hospital; the National Hospital, Queen Square, London; and the Colney Hatch Mental Hospital, London. I wish to express my very great indebtedness and appreciation to the staffs of the above institutions, and especially to Professor Adrian of Cambridge, for their kindness in providing the facilities for this investigation.

REFERENCES.

[1] ADRIAN, E. D., and MATTHEWS, B. H. C. "The Berger Rhythm: Potential Changes from the Occipital Lobes in Man," *Brain*, December, 1934, **57**, 355.

[2] BERGER, HANS. "Das Elektrenkephalogramm des Menschen," *Die Naturwissenschaften*, 1935, **23**, 121.

[3] GIBBS, F. A., DAVIS, H., and LENNOX, W. G. "The Electro-encephalogram in Epilepsy and in Conditions of Impaired Consciousness," *Arch. Neurol. and Psychiat.*, December, 1935, **34**, 1133.

[4] JASPER, H. H., and ANDREWS, H. L. "Human Brain Rhythms. I. Recording Techniques and Preliminary Results," *Journ. Gen. Psychol.*, 1936, **14**, 98.

[5] TÖNNIES, J. F. "Die unipolare Ableitung elektrischer Spannungen vom menschlichen Gehirn," *Die Naturwissenschaften*, February, 1934, **22**, 411..

[6] MATTHEWS, B. H. C. "A Special Purpose Amplifier," *Journ. Physiol.*, March 17, 1934, **81**, 28 P.

[7] BERGER, HANS. "Ueber das Elektrenkephalogramm des Menschen," *Arch. f. Psychiat.*, June, 1935, **103**, 444.

[8] ADRIAN, E. D., and YAMAGIWA, K. "The Origin of the Berger Rhythm," *Brain*, September, 1935, **58**, 323.

[9] FOERSTER, O., and ALTENBURGER, H. "Elektrobiologische Vorgänge ander menschlichen Hirnrinde," *Deutsch. Zeit. f. Nervenheilk.*, 1935, **135**, 277.

A NOTE ON THE PATHOLOGY OF SENILE CHOREA (NON-HEREDITARY).

BY N. S. ALCOCK.

(From the National Hospital, London.)

SENILE chorea has been recognized as an entity by many writers (Collier and Adie [1], Brain [2], Critchley [3]), and may be defined as a condition coming on gradually in late middle life and characterized by generalized choreic movements. It is unaccompanied by mental change, and its onset is usually later in life than that of Huntington's chorea.

These facts would, clinically at any rate, seem to divide it as an entity from Huntington's chorea.

These cases are sometimes, rather unfortunately, known as chronic progressive chorea, although this term is more usually applied to Huntington's chorea. For example Davison [4], who records three cases under this title, takes as his first case one in which there was a clear family history of chorea, the second a doubtful family history of chorea but a plain one of mental changes, and although in his third case there was no family history, yet there was considerable mental change. These, therefore, can only be regarded as cases of Huntington's chorea.

Critchley [3] mentions the condition in his "Neurology of Old Age" and lays down the criteria mentioned above. He states that when these are applied rigidly it is a rarity. He states that the physical signs differ only slightly from those of Sydenham's chorea, except that the movements are perhaps of a wider amplitude, and that a pendular or a sustained knee-jerk is not seen in senile chorea.

He only touches briefly on the pathology of the condition, quoting Jakob [5], who says that senile chorea has been associated with a degeneration of the pallidal, but more particularly of the striatal cells, together with changes in the corpus dentatum. Jakob does not, however, describe clinical cases of senile chorea.

Although it has been recognized by these writers, there is no record of clinical cases with histological studies.

An opportunity presented itself of studying the brains of two patients who, during life, presented only chorea without either mental symptoms or a family history, and who therefore could not be classified as suffering from Huntington's chorea. It is hoped that this study may be of some assistance in elucidating the problem of chorea, especially as this type of case does not seem to have been extensively studied hitherto.

Methods.—It is always difficult to gauge the size of any particular part of the brain in relation to the size of the whole brain. In order, therefore, to estimate the amount of shrinkage of the constituent ganglia of the corpora striata, both in relation to each other and to the normal, the following method was suggested :—

Serial sections of the basal ganglia were cut, stained by Mallory's phosphotungstic acid hæmatoxylin method and their different parts were outlined under a camera lucida with constant magnification ($\times 4\frac{1}{2}$). The area of the different structures in these drawings was then measured by a planimeter. These measurements were then compared with similar sections of three normal brains, which were cut, stained and drawn in the same way. By this simple method it was easy to estimate the size of any nucleus in section, but various facts made it impossible to measure the depth of the nuclei, and therefore the examination was limited to a comparison of their horizontal area.

Intermediate sections were stained by the Nissl, Loyez, Weigert-Pal and hæmatoxylin and van Gieson methods, and sections of the cortex of the frontal, pre- and post-central, and occipital areas, the cornu ammonis, and the pons and mid-brain were cut and stained by the same methods.

Material.—3 normal brains, 2 cases of senile chorea, and 3 cases of Huntington's chorea were examined in this way. In one of the cases of senile chorea a whole brain was available, but in the other only parts could be investigated as it had already been cut for routine examination.

Case 1.—A. F., aged 62, was admitted to the National Hospital under the care of Dr. F. M. R. Walshe in 1926.

Family history.—His father died of tuberculosis. His mother of old age at 75. There was no family history of chorea or insanity.

Past history.—He had an accident in 1924 without loss of consciousness.

History of his present complaint.—During the year before admission to hospital there had been choreic movements which had been generalized from the start. These had increased gradually, but there had been very little progression for three months before admission. Loss of weight had taken place during this year. He was not conscious of any mental deterioration and

stated that his memory was quite good. His sleep had been fitful. The sphincters, ears and eyes, were normal.

On examination at the time of admission, he was an old, poorly nourished man, who went through a series of grotesque choreiform movements. These varied in intensity and were increased under mental or physical effort. They were not the fine movements of a Sydenham's chorea; instead of individual finger movements there was a simultaneous flexion of all the fingers *en bloc*. Movements were most marked in the abdomen, hands and feet. The face seemed relatively less active. There were frequent snarling movements of the lips. The abdominal muscles showed a constant procession of writhing movements. Under strain there was a wild purposeless flail-like slapping about of the forearms.

Speech was extremely difficult to understand as his tongue rolled about in his mouth continually.

Co-ordination tests were well performed, when the chorea was allowed for. There was no rigidity nor spasticity, the tendon-jerks were present and equal, and the plantars were flexor.

He was examined by the psychiatrist attending the hospital, Dr. Bernard Hart, who found that his mental condition was normal.

He remained in very much the same condition and was transferred to another hospital, where he died three years later.

Case 2.—A. B., aged 56, was admitted to St. Charles Hospital, where he died on November 10, 1933.

The notes available from this hospital are unfortunately not so full as in Case 1. There was no family history of chorea or insanity.

He had had choreiform movements of the lips, hands, arms and legs for eight years, which had gradually increased in severity. In addition to this he had some disorder of articulation. There had been no memory loss or mental change.

He was seen there by Dr. J. P. Martin who confirmed the fact that there was no mental change, and on examination noted the generalized chorea, and found that his tendon-jerks were present and equal and that his plantars were flexor; apart from the chorea no abnormal physical signs were detected in the examination of his nervous system.

The Wassermann reaction on the blood was negative.

Measurements.—Portions of the brain of Case 1 had already been embedded in celloidin and mounted on blocks, while the brain in Case 2 had been cut through the basal ganglia by the usual transverse section, and therefore the basal ganglia had to be mounted in two pieces, and it was not possible to estimate the loss of material between the two pieces. It was therefore possible to measure only the horizontal area and to compare the figures obtained with similar measurements of normal brains and of the brains from subjects of Huntington's chorea.

An effort was made to determine accurately the levels of the various sections in the different cases.

Caudate nucleus.—There was little difficulty in comparing the size of this ganglia in different brains as its area only changes from 0·184 to 0·164 square inches, or 0·172 to 0·15 over a depth of 5 mm. in the normal; therefore a very fair comparison can be made.

Comparative readings in square inches of the actual stained structure :—

		Sq. inches		
Three normal brains	..	0·165	0·142	0·175 = Average 0·161
Senile chorea ..	..	Case 1	0·073	
Senile chorea ..	..	Case 2	0·129	
Huntington's chorea	..	Case 1	0·053	
Huntington's chorea	..	Case 2	0·065	

Putamen.—As this structure lies lower than the caudate, the upper limit came within the blocks embedded, so that with a series of sections right through the blocks it was possible to get sections which were the same distance from the top of the putamen.

At lower levels the relative positions of recognizable tracts, as Vicq d'Azyr's bundle, the anterior commissure, &c., were used to determine the levels, and it was found by comparison in the normal cases that levels so determined were nearly correct in all cases.

The readings at three corresponding levels were :—

		Sq. inches		
Level I—				
Three normal brains	..	0·182	0·202	0·193 = Average 0·192
Senile chorea ..	..	Case 1	0·114	
Huntington's chorea	..	Case 1	0·048	
Huntington's chorea	..	Case 2 R.	0·071	
		L.	0·068	
Level II—				
Three normal brains	..	0·376	0·333	0·323 = Average 0·344
Senile chorea ..	..	Case 1	0·182	
Senile chorea ..	..	Case 2	0·296	
Huntington's chorea	..	Case 1	0·113	
(Huntington's chorea	..	Case 3	0·226)[1]	
Level III—				
Three normal brains	..	0·359	0·336	0·321 = Average 0·339
Senile chorea ..	..	Case 1	0·131	
Senile chorea ..	..	Case 2	0·301	
Huntington's chorea	..	Case 1	0·124	
(Huntington's chorea	..	Case 3	0·221)[1]	

[1] Weigert-Pal's method of staining which gives less shrinkage of the material was used. These figures are therefore not really comparable.

The globus pallidus.—This ganglion is spherical in shape and hence slight differences in level make more difference in size of the area than it does in the caudate or putamen. The figures therefore are only approximate. It was, however, possible to obtain a series of sections

through the globus pallidus and the measurements of its area as seen in sections in the different cases were taken at the same distance from the upper margin of the ganglion, where the level was confirmed by the position of the recognizable tracts.

		Sq. inches		
Three normal brains	..	0·161	0·149	0·156 = Average 0·155
Senile chorea ..	..	Case 1	0·121	
Senile chorea ..	..	Case 2	0·107	
Huntington's chorea	..	Case 1	0·079	

Thalamus.—Here the level was fairly easy to determine both by the internal arrangement of its divisions and by its external relations. It also remains the same size through a series of several sections, but varies more than the other structures from one normal to another. The measurements at three different levels are given.

		Sq. inches		
Level I—				
Two normal brains	..	0·211	0·190	= Average 0·201
Huntington's chorea	..	Case 1	0·203	
Huntington's chorea	..	Case 2	0·233	
Level II—				
Two normal brains	..	0·529	0·489	= Average 0·509
Senile chorea ..	..	Case 1	0·544	
Level III—				
Two normal brains		0·462	0·483	= Average 0·473
Senile chorea ..	..	Case 2	0·439	

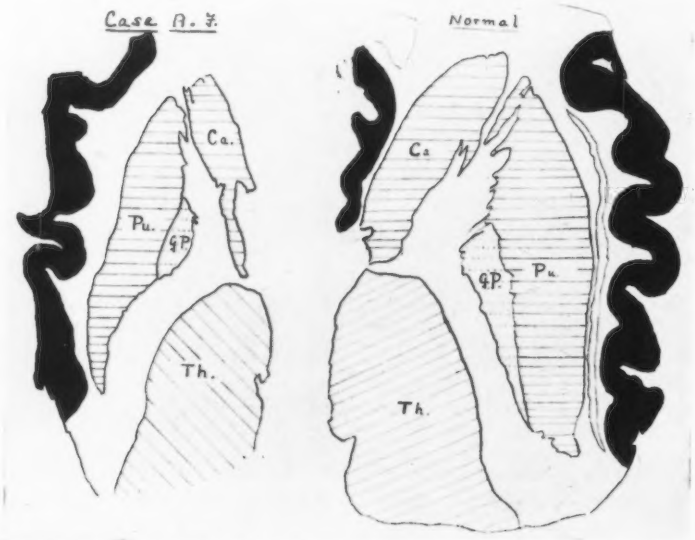

FIG. 1.—The outline of one of the sections of Case 1 for comparison with the drawing of a section through a normal brain at the same level.

PLATE VI.

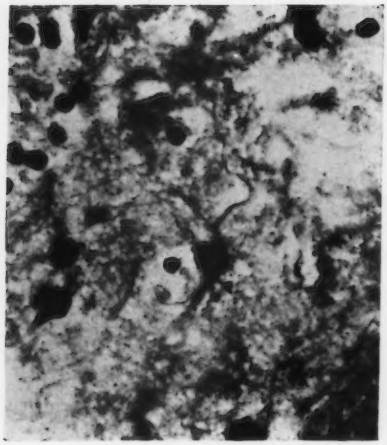

FIG. 1.

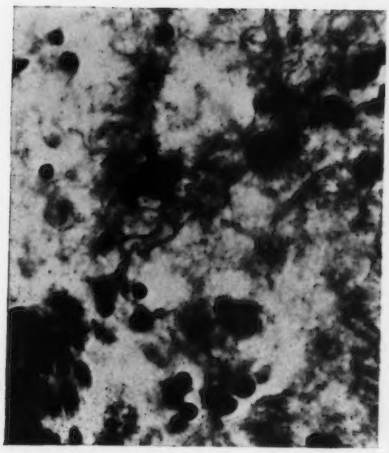

FIG. 2.

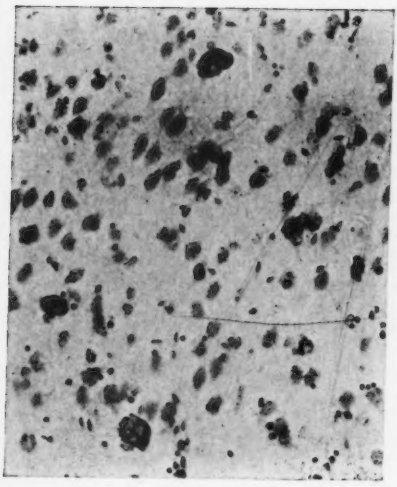

FIG. 3.

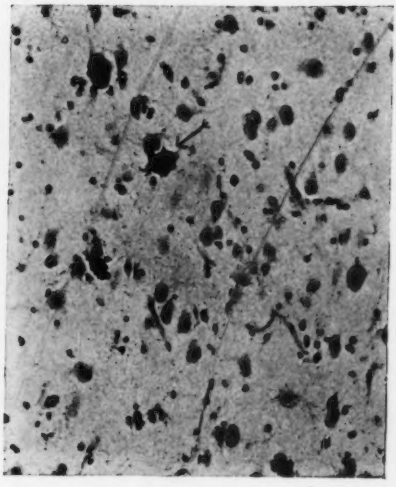

FIG. 4.

FIGS. 1 and 2.—Sections of caudate (fig. 1) and putamen (fig. 2) from Case 1. To show the fibrous astrocytes. Stained by Mallory's phosphotungstic acid hæmatoxylin method. × 500.

FIGS. 3 and 4.—Section of caudate from a normal case (fig. 3) and from Case 1 (fig. 4). To show the degeneration and reduction in number of large and small nerve cells. The arrow points to a large degenerated cell which is packed with pigment. Stained by Nissl's method. × 200.

To illustrate paper by N. S. Alcock.

Microscopical Appearances.

Case 1.—*The Putamen.*—The nerve-cells showed a marked reduction in number: although no cell counts were made, there was no doubt about this. In a normal putamen, in an ordinary field under high power there are always numbers of small cells and one or two large cells, the small cells being, of course, considerably in excess of the large ones. In this case there was only an occasional small cell and several fields had to be searched for a large cell.

The incidence of the affection varied a little from place to place although the difference was not very great. If anything the posterior two-thirds of the putamen tended to show the greatest pathological change.

The appearance of the cells themselves was also greatly altered. The great majority stained poorly, especially with Nissl's method, and their edges were ill-defined. This again varied somewhat from cell to cell; some stained so poorly that they might justifiably be called "shadows," and sometimes the degeneration was so advanced that it became almost a guess that the structure had been a nerve-cell.

An occasional cell, particularly a large cell, had become packed with pigment so that its internal structure was not visible. Such a cell can be seen in the microphotograph of Case 1 (Plate VI, fig. 4). The nuclei also stained poorly and were often eccentric and larger than normal.

These appearances were present in both the large and small cells and it was particularly noted that both were about equally affected. The impression gained from studying several sections was that there was a similar reduction in number of large and small cells.

The neuroglial nuclei were more numerous than in the normal sections, and their marked increase seemed more than could be accounted for by the shrinkage in the size of the whole putamen.

The astrocytes here were particularly interesting. Several of these showed a nucleus and long branching processes which stained well by Mallory's phosphotungstic acid hæmatoxylin method, i.e. the fibrous type of astrocyte. These are not a normal constituent of the putamen, and their presence bears out the contention that there is more change in the glial cells than could be accounted for by shrinkage. (Plate VI, figs. 1 and 2.)

The caudate nucleus.—The pathological changes here were similar to those described in the putamen, but they were less pronounced in its lower part. The upper part of the nucleus was equally severely affected.

There was a similar reduction in number and the same poorly staining degenerated appearance was seen in both the large and small nerve-cells.

The glial changes were also found here, and there was a much greater number of the "spider cell" astrocytes. In the normal caudate there is an occasional fibrous astrocyte near the wall of a blood-vessel and a fairly dense network of these cells line the wall of the ventricle. The same emphasis on their presence does not apply therefore. They were, however, so much in evidence that in the upper part of the caudate in Case 1 the appearance was almost that of a glial scar.

The globus pallidus.—A sudden change of picture is found here. The nerve-cells, which are all large ones, are well stained and had sharp clearly defined edges. Their nuclei which usually lay near the centre of the cell stained normally.

They are obviously more per field than in the normal globus pallidus. This fact and their uniformly healthy appearance leads to the conclusion that the apparent increase in number is accounted for by the shrinkage in the total size of the ganglion.

No pathological change could be seen in the neuroglial elements, beyond a similar increase in their number per field.

Sections stained for myelin on the whole showed very little deviation from the normal. The ansa lenticularis, Forel's H2 bundle, and the fibres crossing the internal capsule from the basal ganglia were all well stained. In some of the sections the ansa appeared a little pale, but this was hardly more than the normal variation from slide to slide.

The only fibres which seemed definitely paler than normal were those that cross the internal capsule lateral to the globus pallidus. These are the only fibres that appear to come from the putamen without first traversing the globus pallidus, and they are normally thinner and paler than the fibres which cross the internal capsule more mesially. In view of this normal variation it is difficult to be certain of the degree of pathological change.

Cerebral cortex.—In the sections studied there was no gross alteration in the appearance of the nerve-cells, and apart from an occasional cell that had not taken up the stain perfectly, they were uniformly healthy in appearance. There was also no alteration in the architecture of the various layers, in fact one would pass the cortex as within normal limits.

The thalamus, corpus Luysii, substantia nigra, mid-brain, pons and cerebellum were studied, the corpus Luysii particularly in view of the

cases in which a lesion of this nucleus is associated with hemi-chorea; but no pathological change was seen in their cells as compared with the normal.

The blood-vessels.—In places these showed some thickening of the wall, but there was no gross change in either case. There was no marked atheroma and no perivascular infiltration of cells.

Case 2.—As has already been noted in this case there was less shrinkage of the basal ganglia. In the putamen, however, there was again a marked reduction in the number of both small and large nerve-cells. Although this reduction was not quite so marked as in Case I the impression was obtained that there was more similarity between the microscopical appearance than would have been expected from the macroscopical picture. Both the large and small cells presented the same degenerated appearance. In this case also no cells were visible that could be regarded as really normal. The globus pallidus contained healthy cells, which seemed to be relatively increased in number in the section.

There was not such a marked increase of neuroglia, but again fibrous astrocytes could easily be found both in putamen and caudate.

Outside the caudate and putamen there was no difference worthy of remark between Case 1 and Case 2. Within these nuclei the changes were merely those of degree. In Case 2 they were not so marked as in Case 1, but the pathological affection seemed to be the same in quality if not in quantity.

Unfortunately the clinical notes do not allow the comparison of the degree of the chorea, and it could not be ascertained whether the chorea in the second case reached the degree it did in the first case. Presumably the more severe histological changes in the first case correspond with the greater degree of shrinkage of these ganglia.

Discussion.

If cases of chorea with mental changes, or with a family history of chorea or mental changes, are excluded, senile chorea is a rare disease. In its early stages the disease progresses, and although it tends to become stationary, the term "chronic progressive chorea" would apply to these cases; but unfortunately this term has been indiscriminately applied both to this condition and to Huntington's chorea, and therefore the term "senile chorea" is to be preferred.

In two conditions in which the chief symptom is so similar, it is to be expected that the pathological picture would also be similar, and this

is what is found. In both conditions there is a gross shrinkage of the basal ganglia. The degree of this varies with the case, but in senile chorea it is not so marked as that found in Huntington's chorea. On an average of the figures, expressed as percentages of the normal, we find that the putamen in senile chorea gave measurements of 45·8 and 72·3 per cent., while in Huntington's chorea it gave 42 per cent.; the caudate in senile chorea gave 54·6 and 77·3 per cent., while in Huntington's chorea it gave the figure of 49 per cent. The globus pallidus gave 75·8 per cent., while in Huntington's chorea it gave 72·75 per cent.

It is interesting to compare the figures obtained by this method with those obtained by Dunlap [6], who made plaster models of the whole of the lenticular nucleus and found this structure in Huntington's chorea as 1 : 2·3 of the normal, i.e. 43·5 per cent.

There is no significant difference between the size of the thalamus in the normal and in senile chorea or Huntington's chorea. This is what would be expected from the normal microscopical picture of the thalamus in these conditions.

As a summary, therefore, we can say that in the basal ganglia, senile chorea shows changes similar to, but of a less degree, than those found in Huntington's chorea. That the various nuclei are affected in the same order; but in each it is a less intense affection.

The chief difference in the microscopical findings between the cases, is that in Huntington's chorea there are pathological changes in the cortex which are not present in senile chorea. This supports the generally accepted view that it is these changes that are responsible for the mental changes in Huntington's chorea, which are absent in senile chorea.

In the basal ganglia the condition is very similar. In both there is a marked affection of the cells of the caudate and putamen. These changes appear to be degenerative in nature, as many of the cells disappear altogether and the remaining ones all show considerable change. The changes tend to be less extreme in senile chorea, which perhaps corresponds with the less progressive nature of the affection. It is noted that although the pathological changes vary from cell to cell, on the whole the incidence is fairly uniform, and that the large and small cells are equally affected.

There is also an overgrowth of the neuroglia in response to these changes, which is shown firstly by the increase in their number and more conclusively by the appearance of types, such as the fibrous astrocytes that are not usually present in this region of the brain.

In the globus pallidus the nerve-cells are unaffected, and it seems therefore reasonable to suppose that the shrinkage in the size of the globus pallidus is due to the degeneration of fibres which normally come from the nerve-cells of the putamen.

The microscopical appearances thus bear out the assumption that senile chorea is dependent on changes similar to those present in Huntington's chorea, but that the process is less advanced. This corresponds with the relative diminution in size of the putamen and caudate nuclei as revealed by measurement. There is, however, the significant difference in the cortex which is unaffected in senile chorea.

On these grounds therefore it is justifiable to separate senile chorea as a pathological as well as a clinical entity from Huntington's chorea.

Ætiology.—We can exclude syphilis as an ætiological factor in these cases, and there is no evidence of a vascular basis for this condition, for no disease was found in the blood-vessels, and in any case a lesion that is so localized does not suggest a widespread cause like vascular disease.

We know that the basal ganglia tend to be affected in certain general diseases, such as hepato-lenticular degeneration in which Wilson [7] suggested an unknown toxin originating in the liver. There is no evidence of any disease of the liver in senile chorea, but it may be that these cases have a toxic origin. There is, however, no evidence in favour of this view, and it appears better to consider them simply as a system degeneration. Whatever the cause may be, it is reasonable to assume that one physiological system is affected.

As both the large and the small cells of the putamen are affected, while those of the globus pallidus escape, it would appear that there is a closer alliance between the large and small cells of the putamen than between the large cells of the putamen and the cells of the globus pallidus. Ramsay Hunt [8] has suggested that the small cells in the putamen belong to one system, and that the large cells in the putamen and in the globus pallidus belong to another, and that with an affection of each system, a particular set of symptoms appear. That disease of the small cells is associated with chorea; of the large cells with striatal rigidity.

Neither the cases of senile chorea nor those of Huntington's chorea support this contention, for it appears improbable that part of the system would show such marked change while the rest appears perfectly healthy.

Additional evidence is afforded by the fact that these cases, and particularly the cases of Huntingtonian chorea, may advance to extreme degrees without showing any lesion in the cells of globus pallidus. The suggestion that all the cells of the putamen are one system and those of the globus pallidus another is supported by Davison [4] and by Winkleman [9] in his discussion on Davison's paper.

The efferent tracts from the basal ganglia consist of the ansa lenticularis, Forel's H2 and the fibres crossing the internal capsule. The ansa and Forel's bundle both appear to come from the globus pallidus and go to the region of the red nucleus, the substantia nigra, the corpus Luysii and neighbouring areas. In the cases I have investigated they do not show any signs of degeneration, and this is additional evidence that they do not come directly from the cells of the putamen.

The fibres that cross the internal capsule may be divided into two parts, the more medial appear to come from the globus pallidus, while the more laterally placed come from the lateral part of the putamen where it is in direct relationship with the internal capsule. These fibres go to form the capsule of the corpus Luysii, and it is these that appear to be paler than normal in the two cases of senile chorea described.

This may be of interest in view of the fact that lesions of the substantia nigra—as in chronic encephalitis lethargica—are associated with the clinical state of Parkinsonism, while lesions of the corpus Luysii are associated with chorea.

The changes in the myelin-stained sections are, however, slight in relation to the changes in the cells, and this would confirm the impression that the chief efferent connections of the putamen, except perhaps those associated with the fibres described, are with the cells of the globus pallidus.

It may be suggested that the incidence of the affection is at one level of the extrapyramidal system, and that this level is represented by the small and large cells of the caudate and putamen, while the other levels, such as the globus pallidus, substantia nigra and other parts of the basal ganglia, are unaffected.

Summary.

(1) Two cases of senile chorea are described with pathological findings.

(2) A new method of mensuration is described.

(3) Comparisons and differences are drawn between Huntington's chorea and senile chorea, and it is suggested that there is sufficient evidence to regard them as different entities.

(4) It is suggested that the small and large cells of the caudate and putamen belong to a different system from those of the globus pallidus.

My thanks are due to Dr. F. M. R. Walshe and Dr. J. Purdon Martin, who have allowed me to use their cases. To Dr. J. G. Greenfield in whose laboratory the work was done, and who throughout gave many suggestions, and to Dr. E. A. Carmichael, who also kindly gave advice.

REFERENCES.

[1] Collier, J., and Adie, W. J. Price, "A Textbook of the Practice of Medicine," London, 1935.
[2] Brain, Russell. "Diseases of the Nervous System," London, 1934.
[3] Critchley, M. *Lancet*, 1931, **1**, 1221.
[4] Davison, C., Goodhart, S. P., and Shlionsky, H. *Arch. Neurol. and Psychiat.*, 1932, **27** 906.
[5] Jakob, A. "Der amyostatische Symptomenkomplex u. verwandte Zustände." *Deut. Zeischr. f. Nervenh.*, 1922, **74**, 47.
[6] Dunlap, C. B. *Arch. Neurol. and Psychiat.*, 1927, **18**, 867.
[7] Wilson, S. A. K. Brain, 1912, **34**, 295.
[8] Hunt, J. R. *Arch. Neurol. and Psychiat.*, 1934, **30**, 1332; Brain, 1917, **40**, 58.
[9] Winkleman, N. W. In discussion on ref. [4]; *Arch. Neurol. and Psychiat.*, 1932. **27**, 1.

Notices of Recent Publications.

Handbuch der Neurologie. Herausgegeben von O. Bumke und O. Foerster. Berlin: Springer, 1936.

The last three volumes of this system of neurology which have been received attain the high level of their predecessors.

BAND IV: *Hirnnerven und Pupille.* S. 701, mit 173 Abbildungen. Price RM. 135.

Short articles by Riese on disturbances of smell by lesions of the olfactory bulbs and olfactory cortex open this volume. Marchesani contributes a full and comprehensive chapter on diseases of the optic nerves, including papill-œdema and retrobulbar neuritis. The two latter conditions are discussed at length, especially with reference to their differential diagnoses. Jaensch's chapter on the investigation of visual function is clear and adequate for the neurologist; he also contributes an excellent article on the pupils. The disturbances of the ocular movements, which was undertaken by Bielschowsky, is perhaps the most striking contribution to the volume; the palsies, ataxias and spasms of the associated movements, as well as the effects of lesions of the oculo-motor nerves, are discussed in a masterly manner, and the subject is presented concisely and clearly. Disorders of vestibular function are demanding more attention in neurology as the important part they play in various reactions of the body is realized, but Klestadt's article of 300 pages on the affections of the nervus acusticus is perhaps out of place in a textbook of this type, although it presents the subject very well. The 20 pages allotted to affection of the other cranial nerves is proportionately meagre.

BAND V: *Rückenmark, Hirnstamm, Kleinhirn.* S. 639, mit 345 Abbildungen. Price RM. 123.

The diseases of the spinal cord and its roots are dealt with by Foerster in the first 400 pages of this volume. It is mainly with the effects of local lesions that he deals, as the systemic and pseudo-systemic diseases are described elsewhere. Every section includes the essential facts of anatomy and physiology; in fact a striking feature of this article, which adds so much to its value, is the presentation of symptoms as disturbances of normal functions. In addition to the motor and sensory disturbances, the disorders of the vegetative system, the reflex disorders and the inco-ordinations and the morbid synergias which result from spinal lesions are fully discussed. The

only criticism which can be raised is the absence of reference to recent work on the bladder and rectum and their sphincters. Lotmar deals with the symptoms associated with disease of the basal ganglia, and Környey with those due to lesions of the brainstem and thalamus. A short but comprehensive and up-to-date article on the symptomatology of the hypothalamus is contributed by Gagel, and Stenvers writes on the postural reflexes. The volume ends with a chapter by Marburg, which might have been profitably lengthened, on the symptoms of cerebellar disease.

BAND X. *Erkrankungen der Wirbelsäule des Schädels mit Nebenhöhlen und der Hüllen.* S. 465, mit 105 Abbildungen. Price RM. 92.

This is a particularly important volume as subjects which often confront the neurologist, but are usually neglected in smaller textbooks, are dealt with excellently here. Lange describes both the commoner and rarer affections of the vertebral column, and Antoni writes on the primary and metastatic tumours involving it. These articles are excellently illustrated. Affections of the scalp and skull are undertaken by Schulze, and Hirsch deals with the intracranial complications of infections of the accessory sinuses. Brunner, a well-known authority on the subject, discusses the intracranial extension of infections from the ear, including cerebral abscesses. Pette contributes a long article on pachymeningitis and leptomeningitis, the most interesting section of which is that on arachnoiditis. The volume ends with an article by Ehrenberg on subarachnoid hæmorrhage.

Pathology of the Nervous System: A Student's Introduction. By J. Henry Biggart. Edinburgh: E. and S. Livingstone. 1936. Pp. 335 with 204 illustrations. Price 15s.

This little book makes no claim to be a complete textbook of neuropathology, but rather to replace and amplify the section on the nervous system in the average textbook of pathology, and to relate this branch of pathology to general pathology. In this it is very successful. The chapter on the neurone is perhaps the most disappointing, as it is too short and condensed to allow of adequate description of the various types of change in the nerve cell, or of the processes of degeneration and repair in the nerve fibre. The other chapters are full enough for their purpose, and those dealing with general processes such as vascular disease and inflammation are excellent. Throughout the book the macroscopic appearances are well described, and questions of pathogenesis in the various diseases are not neglected. The chapters on cerebral and spinal tumours are specially good, and the illustrations here are excellent. Indeed the book is well illustrated throughout both with photographs and drawings. As a whole the book compares very favourably with similar books on neuropathology which have recently appeared in the United States and is very much cheaper.

An Inquiry into Prognosis in the Neuroses. By T. A. Ross. Cambridge: The University Press. 1936. Pp. 192.

It is rare to find a completely dispassionate review and assessment of any mode of medical or surgical treatment, and to seek for it in the literature of the neuroses might seem a singularly unpromising enterprise. Nevertheless, despite the difficulties inherent in the task, Dr. Ross has accomplished it with a remarkable degree of success, and in doing so has laid his professional brethren under a debt of gratitude. In the chaos of conflicting speculations and therapeutic claims that go to swell the monstrous bulk of medical psychological literature, it has become virtually impossible for the ordinary medical reader to separate the grain from the chaff, but in this review of 1,200 cases which have come under his personal observation, Dr. Ross has provided us with a standard by which we may hope to form a reasonable view of the results which skilled and judicious treatment may obtain in the neuroses.

This large series of cases represents the practice of the Cassel Hospital for Functional Nervous Disorders during the period in which Dr. Ross was its Medical Director. His "inquiry" is a model of what such an investigation should be. It cannot be summarized, but one or two striking conclusions may be cited from it:—

(i) Short courses of treatment in which there is no exploration of the infantile unconscious and no formation of a transference which had to be resolved, may be sufficient to bring about character changes of a kind followed by durable improvement in health, and this in other than trivial conditions.

The tacit assumption that anything short of Freudian analysis is useless, is not true.

(ii) The nature of a neurosis does not afford certain evidence as to whether short, or prolonged and analytic treatment will be required.

Each of the main varieties of neurosis is discussed separately, and there are a large number of statistical tables and case histories appended.

This book may be most warmly commended to the attention of neurologists and those psychotherapists who are not neurologists.

The Cerebrospinal Fluid and its Relation to the Blood. By Solomon Katzenelbogen. Baltimore, 1935. The Johns Hopkins Press. Pp. 468. Price 22s. 6d.

This fully documented work covers every aspect of the subject in a full and yet concise manner. The enormous amount of literature which has appeared of recent years is shown by the 44 pages of references at the end of the book, and the author's task in summing up the evidence thus collected must have been a very arduous one. As might be expected from its title, the relation of the chemistry of the spinal fluid to that of the blood forms the chief subject matter and the physical bases of the formation and absorption of the cerebrospinal fluid are only briefly surveyed. Within this limited field the book is remarkably complete, and any omissions of recent important work are readily

explained by the time needed to compile the book. The only criticism that can be made is that the evidence might have been more critically sifted and the author might have used his own judgment more freely in rejecting observations which are either out of date or obviously erroneous. The data given are, however, so abundant that it is usually possible for the reader to correct this fault; if indeed it be a fault to give an observer the benefit of the doubt when it is impossible to check his results. There are also short summaries to many of the chapters in which the author sums up the evidence with a wisdom born of wide experience and intensive research. A comprehensive review of the subject, such as this, will be of great value to those who take a scientific interest in the cerebrospinal fluid.

Handbuch der Biologischen Arbeitsmethoden. Herausgegeben von E. ABDERHALDEN. Urban und Schwartzenberg: Berlin, 1935.

Experimentell-psychologische Schwachsinnsdiagnostik von E. STERN. Abt. VI. Lieferung 448. S. 188. Price RM. 11.

Analyse des Willens. von N. ACH. Abt. VI. Lieferung 446. S. 460. Price RM. 22.

In his preface to the volume in which Dr. Stern's monograph appears, Prof. Abderhalden remarks that there are plenty of problems in applied psychology but no scientific methods which can be used for attacking most of them. This objection does not apply to Dr. Stern's subject which has been carefully investigated by clinical observers and psychologists in many countries. English research is, however, overlooked in this book, e.g. the perceptual tests worked out under Spearman's influence are not mentioned, and the copious American studies receive only the scantiest attention. Apart from this the work is a critical and well arranged guide to intelligence testing and other psychological means of diagnosing mental defect.

Prof. Ach's contribution is on a topic with which his name has been pre-eminently associated for thirty years. Those who have no use for the concept of volition because of their belief in psychological determinism will find here many stubborn experimental facts. Ach's familiar methods of studying the influence of a set task upon the mental processes are fully expounded, with careful discussion of the different viewpoints. The highly technical presentation begins with a general review of the problem and the value of self-observation in studying it: the remaining six chapters deal minutely with "the determining tendency," automatization, monotony, motivation of volitional acts and other subtle questions. It is a book for the expert.

Prognose und Therapie der Geisteskrankheiten. von MAX MULLER. Leipzig: Thieme. 1936. S. 164. Price RM. 7.20.

This is essentially a compendium in which the more recent publications in the German language are reported and arranged in appropriate chapters. The defects of the work may be seen in the section on syphilitic psychoses, in which not a single English or American investigation is mentioned. The

author is an enthusiast about treatment, as his earlier work on the curative mechanisms in schizophrenia had shown. The sections on prognosis are meagre. The author's own views are chiefly given in the chapter on individual psychotherapy, where psychoanalysis is described as the method of choice, with suggestion as a poorer, though often sufficient, alternative and supplement. Among the special chapters are two on epilepsy and drug addictions, but none on the psychoneuroses.

Intelligence, Concrete and Abstract. A Study in Differential Traits. By W. P. ALEXANDER. London: Cambridge University Press. 1935. P. 177. Price 12s. 6d.

The use by Spearman and his pupils of the tetrad method has resulted in much analysis in terms of group factors, but so far no conclusive attempt has been made to resolve performance tests in this way. Dr. Alexander has tried in a painstaking statistical research to remedy this gap in applied psychology. His investigations were made on English and American schoolchildren of various ages and on delinquent women. He concludes that there are factors concerned with practical ability, persistence and the use of numbers, which play an important part in achievement of tasks not predominantly verbal, and he offers in an appendix a suggested use of the tests to measure practical ability. The chief bearing of his research is on education and vocational guidance.

Experimentelle Psychologie in Demonstrationen. von E. BRUNSWIK. Wien: Julius Springer. 1935. S. 166, mit 135 Abbildungen. Price RM. 10.60

The chief merit of this course in experimental psychology lies in the success with which it avoids the use of complicated apparatus. The experiments are designed to give a general survey of the rules and methods of modern psychology, but they will strike the medical reader as cavalier in their treatment of the educational, clinical and social aspects, e.g., the section on "feeling" and emotion is meagre, as is that on intelligence tests. The work is in short academic, but, within its limitations, useful and clear.

The Self in Psychology: A Study in the Foundations of Personality. By A. H. B. ALLEN. Psyche Monographs No. 5. London: Kegan Paul. 1935. Pp. 282. Price 10s. 6d.

The author of this work is widely read in the contemporary literature of psychology but shows limited acquaintance with its methods. His treatment of the topic is on dialectic lines, more akin to philosophy than to any branch of natural science. His main argument is that there is an active central factor or "self" present in all mental life, viewed as an "inner" series of conscious and subconscious events in living human beings. The physical or "outer" series of events he deliberately excludes from his survey.

Basic Problems of Criminology. By OLOF KINBERG. London: William Heinemann. 1935. Pp. 436. Price 20s.

This interesting but diffuse work, of which a great part is devoted to theoretical problems of "imputability," will, responsibility, morality and the purpose of penal law, is reflective rather than clinical. The author devotes two chapters to constitutional and environmental causes, and to the medical and biological aspect of criminal behaviour. He instances the effects of encephalitis lethargica and other brain disease upon conduct, especially sexual conduct, and stresses the importance of the endocrine glands, quoting the assertions of Pende, Vidoni, Berman and others with uncritical favour. In a valuable chapter he described the system of examining prisoners in various European and American States, and makes recommendations on this point, also laying down the general principles of treatment which he thinks desirable. The arguments for sterilization as the most effective means of preventing crime are stated in the last chapter of the book with missionary zeal.

Opicinus de Canistris. Weltbild und Bekenntrisse eines avignonesischen Klerikers des 14. *Jahrhunderts.* von R. Salomon. Textband und Tafelband. London: the Warburg Institute. 1936. Pp. 348 and 89 plates.

The influence of cultural pattern upon the form of mental disorder is well exemplified in the autobiography of Opicinus de Canistris, now for the first time published since it was discovered by Saxl in the Vatican Library in 1913. The autobiography, which has great psychiatric interest, is only one of about two dozen pages of parchment, here beautifully reproduced in the accompanying volume of plates, in which the Pavian cleric gave symbolic and pictorial form to the contents of his mind. The mental disorder under which he laboured when he drew them seems to have been a severe self-reproachful depression, but his productivity was not notably lessened, and there are obsessional and schizophrenic features also. Dr. Salomon's very erudite description and commentary provided the material for a detailed analysis of the structure of this psychosis, so far as it depends on an understanding of the cultural milieu in which the writer lived. There are appended to the main volume a learned examination of the Pavian's artistic method and sources by Heimann, and a note by Krautheimer on the old double cathedral of Pavia which Opicinus has figured. The volume of plates also contains reproductions, a few of them anatomical, from relevant manuscripts and other mediæval works of art.

394

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of "Brain." If reprints are required in pamphlet form, with wrapper, title-page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BALE, SONS & DANIELSSON, Ltd., 83-91, Great Titchfield Street, London, W.

Members of the Neurological Section of the Royal Society of Medicine can obtain the Index of "Brain" for the Volumes I to XXIII inclusive, that is, from its commencement to the end of 1900, from Messrs. MACMILLAN & CO., Ltd., St. Martin's Street, London, W.C., at the price of 6s. 6d., post free.

To those who are not members of the Neurological Section of the Royal Society of Medicine the price is 8s. 6d. net, and the volume may be obtained through any bookseller.

EDITOR.